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21/parts 500-599/989

Food and Drugs

21

PARTS 500 TO 599
Revised as of April 1, 1989



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PARTS 500 TO 599

Revised as of April 1, 1989

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Food and Drug

12

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Cite this Code: CFR

**To cite the regulations in
this volume use title,
part and section
number. Thus, 21 CFR
500.25 refers to Title 21,
Part 500, section 25.**

Explanation

The Code of Federal Regulations is a codification of the general and permanent rules published in the Federal Register by the Executive departments and agencies of the Federal Government. The Code is divided into 50 titles which represent broad areas subject to Federal regulation. Each title is divided into chapters which usually bear the name of the issuing agency. Each chapter is further subdivided into parts covering specific regulatory areas.

ISSUE DATES

Each volume of the Code is revised at least once each calendar year and issued on a quarterly basis approximately as follows:

Title 1 through Title 16.....	as of January 1
Title 17 through Title 27.....	as of April 1
Title 28 through Title 41.....	as of July 1
Title 42 through Title 50.....	as of October 1

The appropriate revision date is printed on the cover of each volume.

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III). A list of CFR Titles, Chapters, and Parts and an alphabetical list of agencies publishing in the CFR are also included in this volume.

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MARTHA L. GIRARD

Acting Director,

Office of the Federal Register.

April 1, 1989.

THIS TITLE

Title 21—FOOD AND DRUGS is composed of nine volumes. The parts in these volumes are arranged in the following order: Parts 1-99, 100-169, 170-199, 200-299, 300-499, 500-599, 600-799, 800-1299, and 1300-End. The first eight volumes, containing Parts 1-1299, comprise Chapter I—Food and Drug Administration, Department of Health and Human Services. The ninth volume, containing Part 1300 to End, includes Chapter II—Drug Enforcement Administration, Department of Justice. The contents of these volumes represent all current regulations codified under this title of the CFR as of April 1, 1989.

The Table of Excepted Prescription Drugs to Part 1308 appears in the volume containing Part 1300-End.

Redesignation tables for Chapter I—Food and Drug Administration appear in the Finding Aids section of the first eight volumes.

For this volume, Loren S. Myers and Doris B. Tucker were Chief Editors. The Code of Federal Regulations publication program is under the direction of Richard L. Claypoole, assisted by Ruth C. Pontius.

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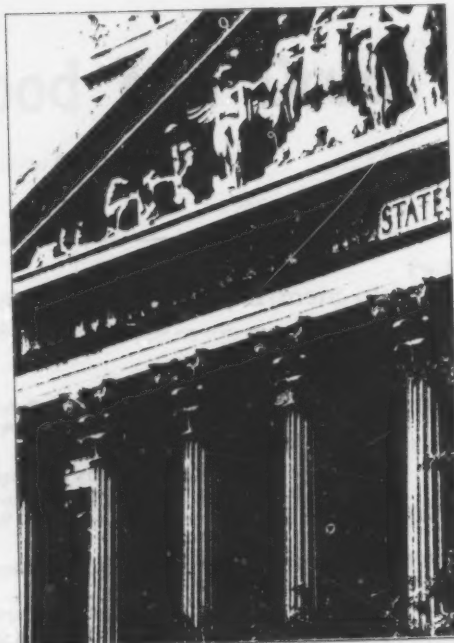
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Title 21—Food and Drugs

(This book contains Parts 500 to 599)

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CROSS REFERENCES:

Animal and Plant Health Inspection Service, Department of Agriculture: See Animals and Animal Products, 9 CFR Chapter I.
Food Safety and Inspection Service, Meat and Poultry Inspection, Department of Agriculture: See Animals and Animal Products, 9 CFR Chapter III.
Federal Trade Commission: See Commercial Practices, 16 CFR Chapter I.
U.S. Customs Service, Department of the Treasury: See Customs Duties, 19 CFR Chapter I.
Internal Revenue Service, Department of the Treasury: See Internal Revenue, 26 CFR Chapter I.
Bureau of Alcohol, Tobacco, and Firearms, Department of the Treasury: See Alcohol, Tobacco Products and Firearms, 27 CFR Chapter I.

CHAPTER I—FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES—

(Continued)

(Parts 500 to 599)

EDITORIAL NOTES: 1. Nomenclature changes affecting this chapter appear at 45 FR 40976, June 17, 1980, and 46 FR 8454, Jan. 27, 1981.

2. The Food and Drug Administration published a document at 49 FR 41019, Oct. 19, 1984, establishing July 1, 1987, as a uniform effective date for compliance for regulations affecting the labeling of food products. At 51 FR 34085, Sept. 25, 1986, FDA established January 1, 1989, as a new uniform effective date for compliance. The new uniform effective date will apply only to final FDA food labeling regulations published after July 1, 1986, and before January 1, 1988.

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- 500.26 Timed-release dosage form drugs.
- 500.27 Methylene blue-containing drugs for use in animals.
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- 500.51 Labeling of animal drugs; misbranding.
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- 500.65 Epinephrine injection 1:1,000 in 10-milliliter containers for emergency treatment of anaphylactoid shock in cattle, horses, sheep, and swine.

Subpart E—Regulation of Carcinogenic Compounds Used in Food-Producing Animals

- 500.80 Scope of this subpart.
- 500.82 Definitions.
- 500.84 Operational definition of no residue.
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- 500.90 Waiver of requirements.
- 500.92 Implementation.

AUTHORITY: Secs. 512, 701(a), 52 Stat. 1055; 82 Stat. 343-351 (21 U.S.C. 360b, 371(a)).

SOURCE: 40 FR 13802, Mar. 27, 1975, unless otherwise noted.

Subpart A—[Reserved]

Subpart B—Specific Administrative Rulings and Decisions

§ 500.25 Anthelmintic drugs for use in animals.

(a) The Commissioner of Food and Drugs has determined that, in order to assure that anthelmintic drugs, including animal feeds bearing or containing such drugs, which do not carry the prescription statement are labeled to provide adequate directions for their effective use, labeling of these anthelmintic drugs shall bear, in addition to other required information, a statement that a veterinarian should be consulted for assistance in the diagnosis, treatment, and control of parasitism.

(b) The label and any labeling furnishing or purporting to furnish directions for use, shall bear conspicuously the following statement: "Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism."

(c) For drugs covered by approved new animal drug applications, the labeling revisions required for compliance with this section may be placed into effect without prior approval as provided for in § 514.8 (d) and (e) of this chapter. For animal feeds bearing or containing anthelmintic drugs covered by approved applications, the labeling revisions required for compliance with this section may be placed into effect without the submission of supplemental applications as provided for in § 514.9 of this chapter.

(d) Labeling revisions required for compliance with this section shall be placed into effect by February 25, 1975, following which, any such drugs that are introduced into interstate commerce and not in compliance with this section will be subject to regulatory proceedings.

§ 500.26 Timed-release dosage form drugs.

(a) Drugs are being offered in dosage forms that are designed to release the

§ 500.27

active ingredients over a prolonged period of time. There is a possibility of unsafe overdosage or ineffective dosage if such products are improperly made and the active ingredients are released at one time, over too short or too long a period of time, or not released at all. Drugs marketed in this form, which are referred to by such terms as timed-release, controlled-release, prolonged-release, sustained-release, or delayed-release drugs, are regarded as new animal drugs within the meaning of section 201(w) of the Federal Food, Drug, and Cosmetic Act.

(b) Timed-release dosage form animal drugs that are introduced into interstate commerce are deemed to be adulterated within the meaning of section 501(a)(5) of the act and subject to regulatory action unless such animal drug is the subject of an approved new animal drug application as required by paragraph (a) of this section.

(c) The fact that the labeling of this kind of drug may claim delayed, prolonged, controlled, or sustained-release of all or only some of the active ingredients does not affect the new animal drug status of such articles. A new animal drug application is required in any such case.

(d) New animal drug applications for timed-release dosage form animal drugs must contain, among other things, data to demonstrate safety and effectiveness by establishing that the article is manufactured using procedures and controls to ensure release of the total dosage at a safe and effective rate. Data submitted in the new animal drug application must demonstrate that the formulation of the drug and the procedures used in its manufacture will ensure release of the active ingredient(s) of the drug at a safe and effective rate and that these release characteristics will be maintained until the expiration date of the drug. When the drug is intended for use in food-producing animals, data submitted must also demonstrate that, with respect to possible residues of the drug, food derived from treated animals is safe for consumption.

[42 FR 8635, Feb. 11, 1977]

21 CFR Ch. I (4-1-89 Edition)

§ 500.27 Methylene blue-containing drugs for use in animals.

(a) New information requires a re-evaluation of the status of drugs containing methylene blue (tetramethylthionine chloride) for oral use in cats or dogs.

(1)(i) It has been demonstrated that two orally administered urinary antiseptic-antispasmodic preparations that contained methylene blue cause Heinz body hemolytic anemia in cats when used according to label directions. The specific cause of the reaction was determined to be the methylene blue contained in the preparations. The reaction can be severe enough to cause death of treated animals.

(ii) The Heinz body hemolytic anemia reaction to methylene blue has also been demonstrated in dogs under laboratory conditions. The precise mechanism by which methylene blue produces the characteristic erythrocytic inclusion bodies (Heinz bodies) and associated hemolytic anemia is unclear.

(2) The effectiveness of orally administered methylene blue as a urinary antiseptic is open to question. It appears that following oral administration, methylene blue is poorly and erratically absorbed and also slowly and erratically excreted in the urine. Studies in the dog indicate it is excreted in the urine essentially as leukomethylene blue stabilized in some manner. Methylene blue itself is stepwise demethylated in alkaline solutions (alkaline urine being a frequent consequence of urinary infection) to Azure B, Azure A, and Azure C. The antiseptic efficacy of all of these excretion products is unsubstantiated.

(3) In view of the foregoing, the Commissioner has concluded that animal drugs containing methylene blue for oral use in cats or dogs are neither safe nor generally recognized as effective within the meaning of section 201(w) of the act and are therefore considered new animal drugs. Accordingly, all prior formal and informal opinions expressed by the Food and Drug Administration that such drugs are "not new drugs" or "no longer new drugs" are hereby revoked.

(b) Animal drugs that contain methylene blue for oral use in cats or dogs and not the subject of an approved new animal drug application (NADA) are deemed to be adulterated under the provisions of section 501(a) (5) and/or (6) and/or misbranded under section 502(a) of the act and subject to regulatory action as of April 10, 1978.

(c) Sponsors of animal drugs that contain methylene blue for oral use in cats or dogs and not the subject of an approved new animal drug application (NADA) may submit an application in conformity with § 514.1 of this chapter. Such applications will be processed in accordance with section 512 of the act. Submission of an NADA will not constitute grounds for continued marketing of this drug substance until such application is approved.

(d) New animal drug applications required by this regulation pursuant to section 512 of the act shall be submitted to the Food and Drug Administration, Bureau of Veterinary Medicine, Office of Scientific Evaluation (HFV-100), 5600 Fishers Lane, Rockville, MD 20857.

[43 FR 9803, Mar. 10, 1978; 43 FR 12310, Mar. 24, 1978]

§ 500.35 Animal feeds contaminated with *Salmonella* microorganisms.

(a) Investigations by the Food and Drug Administration, the Center for Disease Control of the U.S. Public Health Service, the Animal Health Division of the Agricultural Research Service, U.S. Department of Agriculture, and by various State public health agencies have revealed that processed fish meal, poultry meal, meat meal, tankage, and other animal byproducts intended for use in animal feed may be contaminated with *Salmonella* bacteria, an organism pathogenic to man and animals. Contamination of these products may occur through inadequate heat treatment of the product during its processing or through recontamination of the heat-treated product during a time of improper storage or handling subsequent to processing.

(b) Articles used in food for animals are included within the definition of "food" in section 201(f) of the Federal Food, Drug, and Cosmetic Act. Fur-

ther, *Salmonella* contamination of such animal feeds having the potentiality for producing infection and disease in animals must be regarded as an adulterant within the meaning of section 402(a) of the act. Therefore, the Food and Drug Administration will regard as adulterated within the meaning of section 402(a) of the act shipments of the following when intended for animal feed and encountered in interstate commerce and found upon examination to be contaminated with *Salmonella* microorganisms: Bone meal, blood meal, crab meal, feather meal, fish meal, fish solubles, meat scraps, poultry meat meal, tankage, or other similar animal byproducts, or blended mixtures of these.

§ 500.45 Use of polychlorinated biphenyls (PCB's) in the production, handling, and storage of animal feed.

(a) Polychlorinated biphenyls (PCB's) represent a class of toxic industrial chemicals manufactured and sold under a variety of trade names, including: Aroclor (United States); Phenoclor (France); Colphen (Germany); and Kanaclor (Japan). PCB's are highly stable, heat resistant, and non-flammable chemicals. Industrial uses of PCB's include, or did include in the past, their use as electrical transformer and capacitor fluids, heat transfer fluids, hydraulic fluids, plasticizers, and in formulations of lubricants, coatings, and inks. Their unique physical and chemical properties and widespread, uncontrolled industrial applications have caused PCB's to be a persistent and ubiquitous contaminant in the environment, causing the contamination of certain foods. In addition, incidents have occurred in which PCB's have directly contaminated animal feeds as a result of industrial accidents (leakage or spillage of PCB fluids from plant equipment). These accidents in turn cause the contamination of food intended for human consumption (meat, milk, and eggs). Investigations by the Food and Drug Administration have revealed that heat exchange fluids for certain pasteurization equipment used in processing animal feed contain PCB's. Although heat ex-

change fluids in such equipment are considered to be in "closed systems", leakage has occurred that resulted in direct contamination of animal feed with PCB's and subsequently resulted in the transfer of PCB's to human food produced by animals consuming the contaminated feed. The use of PCB-containing coatings on the inner walls of silos has resulted in the contamination of silage which has in turn caused PCB residues in the milk of dairy cows consuming the contaminated silage. Since PCB's are toxic chemicals, the PCB contamination of food as a result of these and other incidents represent a hazard to public health. It is therefore necessary to place certain restrictions on the industrial uses of PCB's in the production, handling, and storage of animal feed.

(b) The following special provisions are necessary to preclude accidental PCB contamination of animal feed:

(1) Coatings or paints for use on the contact surfaces of feed storage areas may not contain PCB's or any other harmful or deleterious substances likely to contaminate feed.

(2) New equipment or machinery for handling or processing feed in or around an establishment producing animal feed shall not contain PCB's.

(3) On or before Sept. 4, 1973, the management of establishments producing animal feed shall:

(i) Have the heat exchange fluid used in existing equipment or machinery for handling and processing feed sampled and tested to determine whether it contains PCB's, or verify the absence of PCB's in such formulations by other appropriate means. On or before Sept. 4, 1973, any such fluid formulated with PCB's must to the fullest extent possible commensurate with current good manufacturing practices, be replaced with a heat exchange fluid that does not contain PCB's.

(ii) Eliminate to the fullest extent possible commensurate with current good manufacturing practices from the animal feed producing establishment any PCB-containing lubricants for equipment or machinery used for handling or processing animal feed.

(iii) Eliminate to the fullest extent possible commensurate with current

good manufacturing practices from the animal feed producing establishment any other PCB-containing materials, whenever there is a reasonable expectation that such materials could cause animal feed to become contaminated with PCB's either as a result of normal use or as a result of accident, breakage, or other mishap.

(iv) The toxicity and other characteristics of fluids selected as PCB replacements must be adequately determined so that the least potentially hazardous replacement should be used. In making this determination with respect to a given fluid, consideration should be given to (a) its toxicity; (b) the maximum quantity that could be spilled onto a given quantity of food before it would be noticed, taking into account its color and odor; (c) possible signaling devices in the equipment to indicate a loss of fluid, etc.; (d) and its environmental stability and tendency to survive and be concentrated through the food chain. The judgment as to whether a replacement fluid is sufficiently non-hazardous is to be made on an individual installation and operation basis.

(c) For the purpose of this section, the provisions do not apply to electrical transformers and condensers containing PCB's in sealed containers.

(d) For the purpose of this section, the term "animal feed" includes all articles used for food or drink for animals other than man.

§ 500.46 Hexachlorophene in animal drugs.

(a) The Commissioner of Food and Drugs has determined that there are no adequate data to establish that animal drugs containing hexachlorophene are safe and effective for any animal use other than in topical products for use on non-food-producing animals as part of a product preservative system at a level not to exceed 0.1 percent; that there is no information on the potential risk to humans from exposure to hexachlorophene by persons who apply animal products containing the drug at levels higher than 0.1 percent; and that there is likewise no information on human exposure to animals on which these animal drugs

have been used and no information on possible residues of hexachlorophene in edible products of food-producing animals treated with new animal drugs that contain any quantity of hexachlorophene.

(b) Animal drugs containing hexachlorophene for other than preservative use on non-food-producing animals at levels not exceeding 0.1 percent are considered new animal drugs and shall be the subject of new animal drug applications (NADA's).

(c) Any person currently marketing animal drugs that contain hexachlorophene other than as part of a product preservative system for products used on non-food-producing animals at a level not exceeding 0.1 percent shall submit a new animal drug application, supplement an existing application, or reformulate the product by September 29, 1977. Each application or supplemental application shall include adequate data to establish that the animal drug is safe and effective. If the animal drug is currently subject to an approved new animal drug application, each reformulation shall require an approved supplemental application. The interim marketing of these animal drugs may continue until the application has been approved, until it has been determined that the application is not approvable under the provisions of § 514.111 of this chapter, or until an existing approved application has been withdrawn.

(d) After September 29, 1977, animal drugs that contain hexachlorophene other than for preservative use on non-food-producing animals at a level not exceeding 0.1 percent that are introduced into interstate commerce shall be deemed to be adulterated within the meaning of section 501(a)(5) of the act (21 U.S.C. 351(a)(5)) unless such animal drug is the subject of a new animal drug application submitted pursuant to paragraph (c) of this section. Action to withdraw approval of new animal drug applications will be initiated if supplemental new animal drug applications have not been submitted in accordance with this section.

(e) New animal drug applications submitted for animal drugs containing hexachlorophene for use in or on

food-producing animals shall include adequate data to assure that edible products from treated animals are safe for human consumption under the labeled conditions of use.

[42 FR 33725, July 1, 1977; 42 FR 37075, July 26, 1977]

§ 500.49 Chlorofluorocarbon propellants.

The use of chlorofluorocarbons as propellants in self-pressurized containers is prohibited from use in all animal drugs, animal food, and related products as provided by § 2.125 of this chapter.

(Secs. 301, 402, 409, 501, 502, 505, 507, 512, 601, 701(a), 52 Stat. 1042-1043 as amended, 1046-1047 as amended, 1049-1054 as amended, 1055, 57 Stat. 463 as amended, 72 Stat. 1785-1788 as amended, 82 stat. 343-351 (21 U.S.C. 331, 342, 348, 351, 352, 355, 357, 360b, 361, 371(a)); sec. 102(2), 83 Stat. 853 (42 U.S.C. 4332))

[43 FR 11317, Mar. 17, 1978]

Subpart C—Animal Drug Labeling Requirements

§ 500.51 Labeling of animal drugs; misbranding.

(a) Among the representations on the label or labeling of an animal drug which will render the drug misbranded are any broad statements suggesting or implying that the drug is not safe and effective for use when used in accordance with labeling direction, or suggesting or implying that the labeling does not contain adequate warnings or adequate directions for use. Such statements include, but are not limited to:

(1) Any statement that disclaims liability when the drug is used in accordance with directions for use contained on the label or labeling.

(2) Any statement that disclaims liability when the drug is used under "abnormal" or "unforeseeable" conditions.

(3) Any statement limiting the warranty for the products to a warranty that the drug in the package contains the ingredients listed on the label.

(b) This regulation is not intended to prohibit any liability disclaimer that purports to limit the amount of damages or that sets forth the legal theory

under which damages are to be recovered.

(c) Any person wishing to obtain an evaluation of an animal drug liability disclaimer under this regulation may submit it to Division of Compliance, (HFV-230), Bureau of Veterinary Medicine, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. A supplemental NADA providing appropriately revised labeling shall be submitted for any approved new animal drug the labeling of which is not in compliance with this regulation.

[41 FR 8473, Feb. 27, 1976]

§ 500.52 Use of terms such as "tonic", "tone", "toner", or "conditioner" in the labeling of preparations intended for use in or on animals.

(a) The use of terms such as "tonic", "tone", "toner", and similar terms in the labeling of a product intended for use in or on animals implies that such product is capable of a therapeutic effect(s) and causes such a product to be a drug within the meaning of section 201(g) of the Federal Food, Drug, and Cosmetic Act. The unqualified use of such terms in a product's labeling fails to provide adequate directions and indications for use of such product and causes it to be misbranded within the meaning of section 502(a) and (f)(1) of the act. The terms "tonic", "tone", "toner", and similar terms may be used in labeling only when appropriately qualified so as to fully inform the user regarding the intended use(s) of the product.

(b) The unqualified use of the term "conditioner" and similar terms in the labeling of a product intended for use in or on animals implies that such product is capable of a therapeutic effect(s) and causes such a product to be a drug within the meaning of section 201(g) of the act. The unqualified use of such terms in a product's labeling fails to provide adequate directions and indications for use of such product and causes it to be misbranded within the meaning of section 502(a) and (f)(1) of the act. The term "conditioner" and similar terms may be used in labeling only when appropriately qualified so as to fully inform the user regarding the intended use(s) of the

product. A product labeled as a "conditioner" or with a similar term can be either a food or drug depending upon the manner in which the term is qualified in the labeling to reflect the product's intended use.

(c) An article so qualified as to be represented as a drug must be the subject of an approved new animal drug application unless the use of the article under the conditions set forth in its labeling is generally recognized as safe and effective among experts qualified by scientific training and experience to evaluate the safety and effectiveness of animal drugs.

§ 500.55 Exemption from certain drug-labeling requirements.

(a) Section 201.105(c) of this chapter provides that in the case of certain drugs for which directions, hazards, warnings, and use information are commonly known to practitioners licensed by law, such information may be omitted from the dispensing package. Under this proviso, the Commissioner of Food and Drugs will offer an opinion, upon written request, stating reasonable grounds therefor on a proposal to omit such information from the dispensing package.

(b) The Commissioner of Food and Drugs has considered submitted material covering a number of drug products and has offered the opinion that the following drugs when intended for those veterinary uses for which they are now generally employed by the veterinary medical profession, should be exempt from the requirements of § 201.105(c) of this chapter, provided that they meet the conditions prescribed in this paragraph. Preparations that are not in dosage unit form (for example, solutions) will be regarded as meeting the conditions with respect to the maximum quantity of drug per dosage unit if they are prepared in a manner that enables accurate and ready administration of a quantity of drug not in excess of the stated maximum per dosage unit:

Atropine sulfate. As an injectable for cattle, goats, horses, pigs, and sheep, not in excess of 15 milligrams per dosage unit; as an injectable for cats and dogs, not in excess of 0.6 milligram per dosage unit.

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Barbital sodium. For oral use in cats and dogs, not in excess of 300 milligrams per dosage unit.

Epinephrine injection. 1:1,000. For cats, dogs, cattle, goats, horses, pigs, and sheep (except as provided in § 500.65).

Morphine sulfate. As an injectable for dogs, not in excess of 15 milligrams per dosage unit.

Pentobarbital sodium. For oral use in cats and dogs, not in excess of 100 milligrams per dosage unit.

Phenobarbital sodium. For oral use in cats and dogs, not in excess of 100 milligrams per dosage unit.

Procaine hydrochloride injection. Containing not in excess of 2 percent procaine hydrochloride, with or without epinephrine up to a concentration of 1:50,000. For use in cats, dogs, cattle, goats, horses, pigs, and sheep.

Thyroid. For oral use in dogs, not in excess of 60 milligrams per dosage unit.

Subpart D—Requirements for Specific Animal Drugs

§ 500.65 Epinephrine injection 1:1,000 in 10-milliliter containers for emergency treatment of anaphylactoid shock in cattle, horses, sheep, and swine.

(a) Anaphylactoid reactions in cattle, horses, sheep, and swine occur occasionally from the injection of antibiotics, bacterins, and vaccines. Adequate directions for use of these antibiotics, bacterins, and vaccines can generally be written for use by the laity and thus are available to livestock producers. Epinephrine injection is effective for the treatment of anaphylactoid reactions in animals and would be of value in saving lives of animals if it were readily available at the time of administration of the causative agents. In connection with this problem the Food and Drug Administration has obtained the views of the Advisory Committee on Veterinary Medicine, and other experts, and has concluded that adequate directions for over-the-counter sale of epinephrine injection 1:1,000 can be prepared.

(b) In view of the above, the Commissioner of Food and Drugs has concluded that it is in the public interest to make epinephrine injection 1:1,000 available for sale without a prescription provided that it is packaged in vials not exceeding 10 milliliters and its label bears, in addition to other re-

quired information, the following statements in a prominent and conspicuous manner: "For emergency use only in treating anaphylactoid shock. Usual Dosage: Cattle, horses, sheep, and swine—1 cubic centimeter per 100 pounds of body weight. Inject subcutaneously".

(c) The labeling must also bear a description of the symptoms of anaphylactoid shock including glassy eyes, increased salivation, grinding of the teeth, rapid breathing, muscular tremors, staggering gait, and collapse with death following. These symptoms may appear shortly after injection of a bacterin, vaccine, or antibiotic.

Subpart E—Regulation of Carcinogenic Compounds Used in Food-Producing Animals

SOURCE: 52 FR 49586, Dec. 31, 1987, unless otherwise noted.

§ 500.80 Scope of this subpart.

(a) The Federal Food, Drug, and Cosmetic Act requires that sponsored compounds intended for use in food-producing animals be shown to be safe and that food produced from animals exposed to these compounds be shown to be safe for consumption by people. The statute prohibits the use in food-producing animals of any compound found to induce cancer when ingested by people or animals unless it can be determined by methods of examination prescribed or approved by the Secretary (a function delegated to the Commissioner of Food and Drugs under § 5.10 of this chapter) that no residue of that compound will be found in the food produced from those animals under conditions of use reasonably certain to be followed in practice. This subpart provides an operational definition of no residue and identifies the steps a sponsor of a compound shall follow to secure the approval of the compound. FDA guidelines contain the procedures and protocols FDA recommends for the implementation of this subpart. These guidelines are available from the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rock-

ville, MD 20857. Requests for these guidelines should be identified with Docket No. 83D-0288.

(b) If FDA concludes on the basis of the threshold assessment that a sponsor shall conduct carcinogenicity testing on the sponsored compound, FDA will also determine whether and to what extent the sponsor shall conduct carcinogenicity testing on metabolites of the sponsored compound. The bioassays that a sponsor conducts must be oral, chronic, dose-response studies and must be designed to assess carcinogenicity and to determine the quantitative aspects of any carcinogenic response.

(c) If FDA concludes on the basis of the threshold assessment or at a later time during the approval process that the data show that the sponsored compound and its metabolites should not be subject to this subpart, FDA will continue to consider the compound for approval under the general safety provisions of the act for risks other than cancer.

(d) This subpart does not apply to essential nutrients.

§ 500.82 Definitions.

(a) The definitions and interpretations contained in section 201 of the act apply to those terms when used in this subpart.

(b) The following definitions apply to this subpart:

"Act" means the Federal Food, Drug, and Cosmetic Act (sections 201-901, 52 Stat. 1040 et seq. as amended (21 U.S.C. 301-392)).

"Essential nutrients" means compounds that are found in the tissues of untreated, healthy target animals and not produced in sufficient quantity to support the animal's growth, development, function, or reproduction, e.g., vitamins, "essential" minerals, "essential" amino acids, and "essential" fatty acids. These compounds must be supplied from external sources.

"FDA" means the Food and Drug Administration.

"Marker residue" means the residue selected for assay whose concentration is in a known relationship to the concentration of the residue of carcinogenic concern in the last tissue to deplete to its permitted concentration.

"Preslaughter withdrawal period" or "milk discard time" means the time after cessation of administration of the sponsored compound for the residue of carcinogenic concern in the edible product to deplete to the concentration that will satisfy the operational definition of no residue.

"Regulatory method" means the aggregate of all experimental procedures for measuring and confirming the presence of the marker residue of the sponsored compound in the target tissue of the target animal.

" R_m " means the concentration of the marker residue in the target tissue when the residue of carcinogenic concern is equal to S_m in the last tissue to deplete to its permitted concentration.

"Residue" means any compound present in edible tissues of the target animal which results from the use of the sponsored compound, including the sponsored compound, its metabolites, and any other substances formed in or on food because of the sponsored compound's use.

"Residue of carcinogenic concern" means all compounds in the total residue of a demonstrated carcinogen excluding any compounds judged by FDA not to present a carcinogenic risk.

" S_m " means the permitted concentration of residue of carcinogenic concern for a specific edible tissue.

" S_0 " means the concentration of the test compound in the total diet of test animals that corresponds to a maximum lifetime risk of cancer in the test animals of 1 in 1 million. For the purpose of this subpart, FDA will also assume that this S_0 will correspond to the concentration of residue of carcinogenic concern in the total human diet that represents no significant increase in the risk of cancer to people.

"Sponsor" means the person or organization proposing or holding an approval by FDA for the use of a sponsored compound.

"Sponsored compound" means any drug or food additive or color additive proposed for use, or used, in food-producing animals or in their feed.

"Target animals" means the production class of animals in which a sponsored compound is proposed or intended for use.

"Target tissue" means the edible tissue selected to monitor for residues in the target animals, including, where appropriate, milk or eggs.

"Test animals" means the species selected for use in the toxicity tests.

"Threshold assessment" means FDA's review of data and information about a sponsored compound to determine whether chronic bioassays in test animals are necessary to resolve questions concerning the carcinogenicity of the compound.

§ 500.84 Operational definition of no residue.

(a) On the basis of the results of the chronic bioassays and other information, FDA will determine whether any of the substances tested are carcinogenic.

(b) If FDA concludes that the results of the bioassays do not establish carcinogenicity, then FDA will not subject the sponsored compound to the remainder of the requirements of this subpart.

(c) For each sponsored compound that FDA decides should be regulated as a carcinogen, FDA will analyze the data from the bioassays using a statistical extrapolation procedure.

(1) For each substance tested in separate bioassays, FDA will calculate the concentration of the residue of carcinogenic concern that corresponds to a maximum lifetime risk to the test animal of 1 in 1 million. FDA will designate the lowest value obtained as S_0 .

(2) FDA will consider that "no residue" of the compound remains in the edible tissue when conditions of use of the sponsored compound, including any required preslaughter withdrawal period or milk discard time, ensure that the concentration of the residue of carcinogenic concern in the total diet of people will not exceed S_0 . Because the total diet is not derived from food-producing animals, FDA will make corrections for food intake. FDA will designate as S_m the concentration of residue of carcinogenic concern that is permitted in a specific edible product.

§ 500.86 Marker residue and target tissue.

(a) For each edible tissue, the sponsor shall measure the depletion of the

residue of carcinogenic concern until its concentration is at or below S_m .

(b) In one or more edible tissues, the sponsor shall also measure the depletion of one or more potential marker residues until the concentration of the residue of carcinogenic concern is at or below S_m .

(c) From these data, FDA will select a target tissue and a marker residue and designate the concentration of marker residue (R_m) that the regulatory method must be capable of measuring in the target tissue. FDA will select R_m such that the absence of the marker residue in the target tissue above R_m can be taken as confirmation that the residue of carcinogenic concern does not exceed S_m in each of the edible tissues and, therefore, that the residue of carcinogenic concern in the diet of people does not exceed S_0 .

(d) When a compound is to be used in milk- or egg-producing animals, milk or eggs must be the target tissue in addition to the tissue selected to monitor for residues in the edible carcass.

(Information collection requirements approved by the Office of Management and Budget under control number 0910-0228)

§ 500.88 Regulatory method.

(a) The sponsor shall submit for evaluation and validation a regulatory method developed to monitor compliance with FDA's operational definition of no residue.

(b) The regulatory method must reliably measure and confirm the identity of the marker residue in the target tissue at concentrations equal to and above R_m .

(c) FDA will publish in the FEDERAL REGISTER the complete regulatory method for measuring the marker residue in the target tissue in accordance with the provisions of sections 409(c)(3)(A), 512(d)(1)(H) and (I), and 706(b)(5)(B) of the act.

(Information collection requirements approved by the Office of Management and Budget under control number 0910-0228)

§ 500.90 Waiver of requirements.

In response to a petition or on the Commissioner's own initiative, the Commissioner may waive, in whole or

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in part, the requirements of this subpart except those provided under § 500.88. A petition for this waiver may be filed by any person who would be adversely affected by the application of the requirements to a particular compound. The petition shall explain and document why the requirements from which a waiver is requested are not reasonably applicable to the compound, and set forth clearly the reasons why the alternative procedures will provide the basis for concluding that approval of the compound satisfies the requirements of the anticancer provisions of the act. If the Commissioner determines that waiver of any of the requirements of this subpart is appropriate, the Commissioner will state the basis for that determination in the regulation approving marketing of the sponsored compound.

(Information collection requirements approved by the Office of Management and Budget under control number 0910-0228)

§ 500.92 Implementation.

(a) This Subpart E applies to all new animal drug applications, food additive petitions, and color additive petitions concerning any compound intended for use in food-producing animals (including supplemental applications and amendments to petitions).

(b) This Subpart E also applies in the following manner to compounds already approved:

(1) For those compounds that FDA determines may induce cancer when ingested by man or animals, i.e., suspect carcinogens, §§ 500.80(b), 500.82, and 500.90 apply.

(2) For those compounds that FDA determines have been shown to induce cancer when ingested by man or animals, §§ 500.82 through 500.90 apply.

PART 501—ANIMAL FOOD LABELING

Subpart A—General Provisions

Sec.

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501.2 Information panel of package for animal food.

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501.3 Identity labeling of animal food in package form.

501.4 Animal food; designation of ingredients.

501.5 Animal food; name and place of business of manufacturer, packer, or distributor.

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501.15 Animal food; prominence of required statements.

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501.22 Animal foods; labeling of spices, flavorings, colorings, and chemical preservatives.

Subparts C-E (Reserved)

Subpart F—Exemptions From Animal Food Labeling Requirements

501.100 Animal food; exemptions from labeling.

501.103 Petitions requesting exemptions from or special requirements for label declaration of ingredients.

501.105 Declaration of net quantity of contents when exempt.

501.110 Animal feed labeling; collective names for feed ingredients.

AUTHORITY: Secs. 4, 6, 80 Stat. 1297, 1299, 1300 (15 U.S.C. 1453, 1455) and secs. 403, 602, 701, 52 Stat. 1047-1048 as amended, 1054-1056 as amended (21 U.S.C. 343, 362, 371).

SOURCE: 41 FR 38619, Sept. 10, 1976, unless otherwise noted.

Subpart A—General Provisions

§ 501.1 Principal display panel of package form animal food.

The term "principal display panel" as it applies to food in package form and as used in this part, means the part of a label that is most likely to be displayed, presented, shown, or examined under customary conditions of display for retail sale. The principal display panel shall be large enough to accommodate all the mandatory label information required to be placed thereon by this part with clarity and conspicuousness and without obscuring design, vignettes, or crowding.

Where packages bear alternate principal display panels, information required to be placed on the principal display panel shall be duplicated on each principal display panel. For the purpose of obtaining uniform type size in declaring the quantity of contents for all packages of substantially the same size, the term "area of the principal display panel" means the area of the side or surface that bears the principal display panel, which area shall be:

(a) In the case of a rectangular package where one entire side properly can be considered to be the principal display panel side, the product of the height times the width of that side;

(b) In the case of a cylindrical or nearly cylindrical container, 40 percent of the product of the height of the container times the circumference;

(c) In the case of any otherwise shaped container, 40 percent of the total surface of the container: *Provided, however*, That where such container presents an obvious "principal display panel" such as the top of a triangular or circular package, the area shall consist of the entire top surface. In determining the area of the principal display panel, exclude tops, bottoms, flanges at tops and bottoms of cans, and shoulders and necks of bottles or jars. In the case of cylindrical or nearly cylindrical containers, information required by this part to appear on the principal display panel shall appear within that 40 percent of the circumference which is most likely to be displayed, presented, shown, or examined under customary conditions of display for retail sale.

§ 501.2 Information panel of package for animal food.

(a) The term "information panel" as it applies to packaged food means that part of the label immediately contiguous and to the right of the principal display panel as observed by an individual facing the principal display panel with the following exceptions:

(1) If the part of the label immediately contiguous and to the right of the principal display panel is too small to accommodate the necessary information or is otherwise unusable label space, e.g., folded flaps or can ends,

the panel immediately contiguous and to the right of this part of the label may be used.

(2) If the package has one or more alternate principal display panels, the information panel is immediately contiguous and to the right of any principal display panel.

(3) If the top of the container is the principal display panel and the package has no alternate principal display panel, the information panel is any panel adjacent to the principal display panel.

(b) All information required to appear on the label of any package of food pursuant to §§ 501.4, 501.5, 501.8 and 501.17 shall appear either on the principal display panel or on the information panel, unless otherwise specified by regulations in this chapter.

(c) All information appearing on the principal display panel or the information panel pursuant to this section shall appear prominently and conspicuously, but in no case may the letters and/or numbers be less than $\frac{1}{16}$ inch in height unless an exemption pursuant to paragraph (f) of this section is established. The requirements for conspicuousness and legibility shall include the specifications of §§ 501.15 and 501.105(h) (1) and (2).

(1) Packaged foods are exempt from the type size requirements of this paragraph: *Provided, That:*

(i) The package is designed such that it has a surface area that can bear an information panel and/or an alternate principal display panel.

(ii) The area of surface available for labeling on the principal display panel of the package as this term is defined in § 501.1 is less than 10 square inches.

(iii) The label information includes a full list of ingredients in accordance with regulations in this part.

(iv) The information required by paragraph (b) of this section appears on the principal display panel or information panel label in accordance with the provisions of this paragraph (c) except that the type size is not less than $\frac{1}{16}$ inch in height.

(2) Packaged foods are exempt from the type size requirements of this paragraph: *Provided, That:*

(i) The package is designed such that it has a single "obvious principal

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display panel" as this term is defined in § 501.1 and has no other available surface area for an information panel or alternate principal display panel.

(ii) The area of surface available for labeling on the principal display panel of the package as this term is defined in § 501.1 is less than 12 square inches and bears all labeling appearing on the package.

(iii) The label information includes a full list of ingredients in accordance with regulations in this part.

(iv) The information required by paragraph (b) of this section appears on the single, obvious principal display panel in accordance with the provisions of this paragraph (c) except that the type size is not less than $\frac{1}{32}$ inch in height.

(3) Packaged foods are exempt from the type size requirements of this paragraph: *Provided, That:*

(i) The package is designed such that it has a total surface area available to bear labeling of less than 12 square inches.

(ii) The label information includes a full list of ingredients in accordance with regulations in this part.

(iii) The information required by paragraph (b) of this section appears on the principal display panel or information panel label in accordance with the provisions of this paragraph (c) except that the type size is not less than $\frac{1}{32}$ inch in height.

(d) All information required to appear on the principal display panel or on the information panel pursuant to this section shall appear on the same panel unless there is insufficient space. In determining the sufficiency of the available space, any vignettes, design, and other nonmandatory label information shall not be considered. If there is insufficient space for all of this information to appear on a single panel, it may be divided between these two panels except that the information required pursuant to any given section or part shall all appear on the same panel. A food whose label is required to bear the ingredient statement on the principal display panel may bear all other information specified in paragraph (b) of this section on the information panel.

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(e) All information appearing on the information panel pursuant to this section shall appear in one place without other intervening material.

(f) If the label of any package of food is too small to accommodate all of the information required by §§ 501.4, 501.5, 501.8, and 501.17, the Commissioner may establish by regulation an acceptable alternative method of disseminating such information to the public, e.g., a type size smaller than one-sixteenth inch in height, or labeling attached to or inserted in the package or available at the point of purchase. A petition requesting such a regulation, as an amendment to this paragraph shall be submitted pursuant to Part 10 of this chapter.

[41 FR 38619, Sept. 10, 1976, as amended at 42 FR 4716, Jan. 25, 1977; 42 FR 15675, Mar. 22, 1977]

§ 501.3 Identity labeling of animal food in package form.

(a) The principal display panel of a food in package form shall bear as one of its principal features a statement of the identity of the commodity.

(b) Such statement of identity shall be in terms of:

(1) The name now or hereafter specified in or required by any applicable Federal law or regulation; or, in the absence thereof,

(2) The common or usual name of the food; or, in the absence thereof,

(3) An appropriately descriptive term, or when the nature of the food is obvious, a fanciful name commonly used by the public for such food.

(c) Where a food is marketed in various optional forms (whole, slices, diced, etc.), the particular form shall be considered to be a necessary part of the statement of identity and shall be declared in letters of a type size bearing a reasonable relation to the size of the letters forming the other components of the statement of identity; except that if the optional form is visible through the container or is depicted by an appropriate vignette, the particular form need not be included in the statement. This specification does not affect the required declarations of identity under definitions and stand-

ards for foods promulgated pursuant to section 401 of the act.

(d) This statement of identity shall be presented in bold type on the principal display panel, shall be in a size reasonably related to the most prominent printed matter on such panel, and shall be in lines generally parallel to the base on which the package rests as it is designed to be displayed.

(e) Under the provisions of section 403(c) of the Federal Food, Drug, and Cosmetic Act, a food shall be deemed to be misbranded if it is an imitation of another food unless its label bears, in type of uniform size and prominence, the word "imitation" and, immediately thereafter, the name of the food imitated.

(1) A food shall be deemed to be an imitation and thus subject to the requirements of section 403(c) of the act if it is a substitute for and resembles another food but is nutritionally inferior to that food.

(2) A food that is a substitute for and resembles another food shall not be deemed to be an imitation provided it meets each of the following requirements:

(i) It is not nutritionally inferior to the food for which it substitutes and which it resembles.

(ii) Its label bears a common or usual name that complies with the provisions of § 502.5 of this chapter and that is not false or misleading, or in the absence of an existing common or usual name, an appropriately descriptive term that is not false or misleading. The label may, in addition, bear a fanciful name which is not false or misleading.

(3) A food for which a common or usual name is established by regulation (e.g., in a standard of identity pursuant to section 401 of the act, in a common or usual name regulation pursuant to false or misleading. The label may, in addition, bear a fanciful name which is Part 502 of this chapter), and which complies with all of the applicable requirements of such regulation(s), shall not be deemed to be an imitation.

(4) Nutritional inferiority includes:

(i) Any reduction in the content of an essential nutrient that is present in a measurable amount.

(ii) If the Commissioner concludes that a food is a substitute for and resembles another food but is inferior to the food imitated for reasons other than those set forth in this paragraph, he may propose appropriate revisions to this regulation or he may propose a separate regulation governing the particular food.

(f) A label may be required to bear the percentage(s) of a characterizing ingredient(s) or information concerning the presence or absence of an ingredient(s) or the need to add an ingredient(s) as part of the common or usual name of the food pursuant to Part 502 of this chapter.

[41 FR 38619, Sept. 10, 1976, as amended at 42 FR 14091, Mar. 15, 1977]

§ 501.4 Animal food; designation of ingredients.

(a) Ingredients required to be declared on the label of a food, including foods that comply with standards of identity that require labeling in compliance with this Part 501, except those exempted by § 501.100, shall be listed by common or usual name in descending order of predominance by weight on either the principal display panel or the information panel in accordance with the provisions of § 501.2.

(b) The name of an ingredient shall be a specific name and not a collective (generic) name, except that:

(1) Spices, flavorings, colorings and chemical preservatives shall be declared according to the provisions of § 501.22.

(2) An ingredient which itself contains two or more ingredients and which has an established common or usual name, conforms to a standard established pursuant to the Meat Inspection or Poultry Products Inspection Acts by the U.S. Department of Agriculture, or conforms to a definition and standard of identity established pursuant to section 401 of the Federal Food, Drug, and Cosmetic Act, shall be designated in the statement of ingredients on the label of such food by either of the following alternatives:

(i) By declaring the established common or usual name of the ingredient followed by a parenthetical listing

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of all ingredients contained therein in descending order of predominance except that, if the ingredient is a food subject to a definition and standard of identity established in this subchapter E, only the ingredients required to be declared by the definition and standard of identity need be listed; or

(ii) By incorporating into the statement of ingredients in descending order of predominance in the finished food, the common or usual name of every component of the ingredient without listing the ingredient itself.

(3) Skim milk, concentrated skim milk, reconstituted skim milk, and nonfat dry milk may be declared as "skim milk" or "nonfat milk".

(4) Milk, concentrated milk, reconstituted milk, and dry whole milk may be declared as "milk".

(5) Bacterial cultures may be declared by the word "cultured" followed by the name of the substrate, e.g., "made from cultured skim milk or cultured buttermilk".

(6) Sweetcream buttermilk, concentrated sweetcream buttermilk, reconstituted sweetcream buttermilk, and dried sweetcream buttermilk may be declared as "buttermilk".

(7) Whey, concentrated whey, reconstituted whey, and dried whey may be declared as "whey".

(8) Cream, reconstituted cream, dried cream, and plastic cream (sometimes known as concentrated milkfat) may be declared as "cream".

(9) Butteroil and anhydrous butterfat may be declared as "butterfat".

(10) Dried whole eggs, frozen whole eggs, and liquid whole eggs may be declared as "eggs".

(11) Dried egg whites, frozen egg whites, and liquid egg whites may be declared as "egg whites".

(12) Dried egg yolks, frozen egg yolks, and liquid egg yolks may be declared as "egg yolks".

(13) A livestock or poultry feed may be declared by a collective name listed in § 501.110 if it is an animal feed within the meaning of section 201(x) of the act and meets the requirements for the use of a collective name as prescribed in § 501.110 for certain feed ingredients.

(14) [Reserved]

(15) When all the ingredients of a wheat flour are declared in an ingredient statement, the principal ingredient of the flour shall be declared by the name(s) specified in §§ 137.105, 137.200, 137.220, 137.225 of this chapter, i.e., the first ingredient designated in the ingredient list of flour, or bromated flour, or enriched flour, or self-rising flour is "flour", "white flour", "wheat flour", or "plain flour"; the first ingredient designated in the ingredient list of durum flour is "durum flour"; the first ingredient designated in the ingredient list of whole wheat flour, or bromated whole wheat flour is "whole wheat flour", "graham flour", or "entire wheat flour"; and the first ingredient designated in the ingredient list of whole durum wheat flour is "whole durum wheat flour".

(c) When water is added to reconstitute, completely or partially, an ingredient permitted by paragraph (b) of this section to be declared by a class name, the position of the ingredient class name in the ingredient statement shall be determined by the weight of the unreconstituted ingredient plus the weight of the quantity of water added to reconstitute that ingredient, up to the amount of water needed to reconstitute the ingredient to single strength. Any water added in excess of the amount of water needed to reconstitute the ingredient to single strength shall be declared as "water" in the ingredient statement.

[41 FR 38619, Sept. 10, 1976, as amended at 42 FR 14091, Mar. 15, 1977]

§ 501.5 Animal food; name and place of business of manufacturer, packer, or distributor.

(a) The label of a food in packaged form shall specify conspicuously the name and place of business of the manufacturer, packer, or distributor.

(b) The requirement for declaration of the name of the manufacturer, packer, or distributor shall be deemed to be satisfied, in the case of a corporation, only by the actual corporate name, which may be preceded or followed by the name of the particular division of the corporation. In the case of an individual, partnership, or asso-

ciation, the name under which the business is conducted shall be used.

(c) Where the food is not manufactured by the person whose name appears on the label, the name shall be qualified by a phrase that reveals the connection such person has with such food; such as "Manufactured for _____," "Distributed by _____," or any other wording that expresses the facts.

(d) The statement of the place of business shall include the street address, city, State, and ZIP Code; however, the street address may be omitted if it is shown in a current city directory or telephone directory. The requirement for inclusion of the ZIP Code shall apply only to consumer commodity labels developed or revised after the effective date of this section. In the case of nonconsumer packages, the ZIP Code shall appear either on the label or the labeling (including invoice).

(e) If a person manufactures, packs, or distributes a food at a place other than his principal place of business, the label may state the principal place of business in lieu of the actual place where such food was manufactured or packed or is to be distributed, unless such statement would be misleading.

§ 501.8 Labeling of animal food with number of servings.

(a) The label of any package of a food which bears a representation as to the number of servings contained in such package shall bear in immediate conjunction with such statement, and in the same size type as is used for such statement, a statement of the net quantity (in terms of weight, measure, or numerical count) of each such serving; however, such statement may be expressed in terms that differ from the terms used in the required statement of net quantity of contents (for example, cupfuls, tablespoonfuls, etc.) when such differing term is common to cookery and describes a constant quantity. Such statement may not be misleading in any particular. A statement of the number of units in a package is not in itself a statement of the number of servings.

(b) If there exists a voluntary product standard promulgated pursuant to

the procedures found in 15 CFR Part 10 by the Department of Commerce, quantitatively defining the meaning of the term "serving" with respect to a particular food, then any label representation as to the number of servings in such packaged food shall correspond with such quantitative definition. (Copies of published standards are available upon request from the National Bureau of Standards, Department of Commerce, Washington, DC 20234.)

§ 501.15 Animal food; prominence of required statements.

(a) A word, statement, or other information required by or under authority of the act to appear on the label may lack that prominence and conspicuousness required by section 403(f) of the act by reason (among other reasons) of:

(1) The failure of such word, statement, or information to appear on the part or panel of the label which is presented or displayed under customary conditions of purchase;

(2) The failure of such word, statement, or information to appear on two or more parts or panels of the label, each of which has sufficient space therefor, and each of which is so designed as to render it likely to be, under customary conditions of purchase, the part or panel displayed;

(3) The failure of the label to extend over the area of the container or package available for such extension, so as to provide sufficient label space for the prominent placing of such word, statement, or information;

(4) Insufficiency of label space (for the prominent placing of such word, statement, or information) resulting from the use of label space for any word, statement, design, or device which is not required by or under authority of the act to appear on the label;

(5) Insufficiency of label space (for the prominent placing of such word, statement, or information) resulting from the use of label space to give materially greater conspicuousness to any other word, statement, or information, or to any design or device; or

(6) Smallness or style of type in which such word, statement, or information appears, insufficient background contrast, obscuring designs or vignettes, or crowding with other written, printed, or graphic matter.

(b) No exemption depending on insufficiency of label space, as prescribed in regulations promulgated under section 403(e) or (i) of the act, shall apply if such insufficiency is caused by:

(1) The use of label space for any word, statement, design, or device which is not required by or under authority of the act to appear on the label;

(2) The use of label space to give greater conspicuousness to any word, statement, or other information that is required by section 403(f) of the act; or

(3) The use of label space for any representation in a foreign language.

(c)(1) All words, statements, and other information required by or under authority of the act to appear on the label or labeling shall appear thereon in the English language: *Provided, however*, That in the case of articles distributed solely in the Commonwealth of Puerto Rico or in a Territory where the predominant language is one other than English, the predominant language may be substituted for English.

(2) If the label contains any representation in a foreign language, all words, statements, and other information required by or under authority of the act to appear on the label shall appear thereon in the foreign language.

(3) If any article of labeling (other than a label) contains any representation in a foreign language, all words, statements, and other information required by or under authority of the act to appear on the label or labeling shall appear on such article of labeling.

§ 501.17 Animal food labeling warning statements.

(a) *Self-pressurized containers.* (1) The label of a food packaged in a self-pressurized container and intended to be expelled from the package under

pressure shall bear the following warning:

Warning—Avoid spraying in eyes. Contents under pressure. Do not puncture or incinerate. Do not store at temperature above 120° F. Keep out of reach of children.

(2) In the case of products intended for use by children, the phrase "except under adult supervision" may be added at the end of the last sentence in the warning required by paragraph (a)(1) of this section.

(3) In the case of products packaged in glass containers, the word "break" may be substituted for the word "puncture" in the warning required by paragraph (a)(1) of this section.

(4) The words "Avoid spraying in eyes" may be deleted from the warning required by paragraph (a)(1) of this section in the case of a product not expelled as a spray.

(b) *Self-pressurized containers with halocarbon or hydrocarbon propellants.* (1) In addition to the warning required by paragraph (a) of this section, the label of a food packaged in a self-pressurized container in which the propellant consists in whole or in part of a halocarbon or a hydrocarbon shall bear the following warning:

Warning—Use only as directed. Intentional misuse by deliberately concentrating and inhaling the contents can be harmful or fatal.

(2) The warning required by paragraph (b)(1) of this section is not required for the following products:

(i) Products expelled in the form of a foam or cream, which contain less than 10 percent propellant in the container.

(ii) Products in a container with a physical barrier that prevents escape of the propellant at the time of use.

(iii) Products of a net quantity of contents of less than 2 ozs that are designed to release a measured amount of product with each valve actuation.

(iv) Products of a net quantity of contents of less than ¼ oz.

(c) *Self-pressurized containers with a chlorofluorocarbon propellant.* (1) In addition to the warning required by paragraphs (a) and (b) of this section, the label on each package of a food in a self-pressurized container in which the propellant consists in whole or in

part of a fully halogenated chloroalkane (chlorofluorocarbon) shall bear the following warning:

Warning—Contains a chlorofluorocarbon that may harm the public health and environment by reducing the ozone in the upper atmosphere.

(2) The warning required by paragraph (c)(1) of this section shall appear on an appropriate panel with such prominence and conspicuousness as to render it likely to be read and understood by ordinary individuals under normal conditions of purchase. The warning may appear on a firmly affixed tag, tape, card, or sticker or similar overlabeling attached to the package. The warning shall comply in all other respects with § 501.2, e.g., type-size requirements.

(3) The warning required by paragraph (c)(1) of this section is applicable only to self-pressurized containers that use a chlorofluorocarbon in whole or in part as a propellant to expel from the container liquid or solid material different from the propellant.

(Secs. 201(n), 301, 402, 403, 501, 502, 505, 507, 512, 601, 602, 701(a), 52 Stat. 1041-1043 as amended, 1046-1048 as amended, 1049, 1051-1053 as amended, 1054-1055, 57 Stat. 463 as amended, 82 Stat. 343-351 (21 U.S.C. 321(n), 331, 342, 343, 351, 352, 355, 357, 360b, 361, 362, and 371(a)); sec. 102(2), 83 Stat. 853 (42 U.S.C. 4332); 21 CFR 5.1)

[41 FR 38619, Sept. 10, 1976, as amended at 42 FR 22033, Apr. 29, 1977]

§ 501.18 Misbranding of animal food.

(a) Among representations in the labeling of a food which render such food misbranded is a false or misleading representation with respect to another food or a drug, device, or cosmetic.

(b) The labeling of a food which contains two or more ingredients may be misleading by reason (among other reasons) of the designation of such food in such labeling by a name which includes or suggests the name of one or more but not all such ingredients, even though the names of all such ingredients are stated elsewhere in the labeling.

(c) Among representations in the labeling of a food which render such food misbranded is any representation

that expresses or implies a geographical origin of the food or any ingredient of the food except when such representation is either:

(1) A truthful representation of geographical origin.

(2) A trademark or trade name provided that as applied to the article in question its use is not deceptively misdescriptive. A trademark or trade name comprised in whole or in part of geographical words shall not be considered deceptively misdescriptive if it:

(i) Has been so long and exclusively used by a manufacturer or distributor that it is generally understood by the consumer to mean the product of a particular manufacturer or distributor; or

(ii) Is so arbitrary or fanciful that it is not generally understood by the consumer to suggest geographic origin.

(3) A part of the name required by applicable Federal law or regulation.

(4) A name whose market significance is generally understood by the consumer to connote a particular class, kind, type, or style of food rather than to indicate geographical origin.

Subpart B—Specific Animal Food Labeling Requirements

§ 501.22 Animal foods; labeling of spices, flavorings, colorings, and chemical preservatives.

(a)(1) The term "artificial flavor" or "artificial flavoring" means any substance, the function of which is to impart flavor, which is not derived from a spice, fruit or fruit juice, vegetable or vegetable juice, edible yeast, herb, bark, bud, root, leaf or similar plant material, meat, fish, poultry, eggs, dairy products, or fermentation products thereof. Artificial flavor includes the substances listed in §§ 172.515(b) and 582.60 of this chapter except where these are derived from natural sources.

(2) The term "spice" means any aromatic vegetable substance in the whole, broken, or ground form, except for those substances which have been traditionally regarded as foods, such as onions, garlic and celery; whose significant function in food is seasoning rather than nutritional; that is true to

name; and from which no portion of any volatile oil or other flavoring principle has been removed. Spices include the spices listed in Subpart A of Part 582 of this chapter, such as the following:

Allspice, Anise, Basil, Bay leaves, Caraway seed, Cardamon, Celery seed, Chervil, Cinnamon, Cloves, Coriander, Cumin seed, Dill seed, Fennel seed, Fenugreek, Ginger, Horseradish, Mace, Marjoram, Mustard flour, Nutmeg, Oregano, Paprika, Parsley, Pepper, black; Pepper, white; Pepper, red; Rosemary, Saffron, Sage, Savory, Star aniseed, Tarragon, Thyme, Turmeric.

Paprika, turmeric, and saffron or other spices which are also colors, shall be declared as "spice and coloring" unless declared by their common or usual name.

(3) The term "natural flavor" or "natural flavoring" means the essential oil, oleoresin, essence or extractive, protein hydrolysate, distillate, or any product of roasting, heating or enzymolysis, which contains the flavoring constituents derived from a spice, fruit or fruit juice, vegetable or vegetable juice, edible yeast, herb, bark, bud, root, leaf or similar plant material, meat, seafood, poultry, eggs, dairy products, or fermentation products thereof, whose significant function in food is flavoring rather than nutritional. Natural flavors include the natural essence or extractives obtained from plants listed in Subpart A of Part 582 of this chapter, and the substances listed in § 172.510 of this chapter.

(4) The term "artificial color" or "artificial coloring" means any "color additive" as defined in § 70.3(f) of this chapter.

(5) The term "chemical preservative" means any chemical that, when added to food, tends to prevent or retard deterioration thereof, but does not include common salt, sugars, vinegars, spices, or oils extracted from spices, substances added to food by direct exposure thereof to wood smoke, or chemicals applied for their insecticidal or herbicidal properties.

(b) A food which is subject to the requirements of section 403(k) of the act shall bear labeling, even though such food is not in package form.

(c) A statement of artificial flavoring, artificial coloring, or chemical pre-

servative shall be placed on the food, or on its container or wrapper, or on any two or all of these, as may be necessary to render such statement likely to be read by the ordinary individual under customary conditions of purchase and use of such food.

(d) A food shall be exempt from compliance with the requirements of section 403(k) of the act if it is not in package form and the units thereof are so small that a statement of artificial flavoring, artificial coloring, or chemical preservative, as the case may be, cannot be placed on such units with such conspicuousness as to render it likely to be read by the ordinary individual under customary conditions of purchase and use.

(e) A food shall be exempt while held for sale from the requirements of section 403(k) of the act (requiring label statement of any artificial flavoring, artificial coloring, or chemical preservatives) if said food, having been received in bulk containers at a retail establishment, is displayed to the purchaser with either (1) the labeling of the bulk container plainly in view or (2) a counter card, sign, or other appropriate device bearing prominently and conspicuously the information required to be stated or the label pursuant to section 403(k) of the act.

(f) A fruit or vegetable shall be exempt from compliance with the requirements of section 403(k) of the act with respect to a chemical preservative applied to the fruit or vegetable as a pesticide chemical prior to harvest.

(g) A flavor shall be labeled in the following way when shipped to a food manufacturer or processor (but not a consumer) for use in the manufacture of a fabricated food, unless it is a flavor for which a standard of identity has been promulgated, in which case it shall be labeled as provided in the standard:

(1) If the flavor consists of one ingredient, it shall be declared by its common or usual name.

(2) If the flavor consists of two or more ingredients, the label either may declare each ingredient by its common or usual name or may state "All flavor ingredients contained in this product are approved for use in a regulation of the Food and Drug Administration."

Any flavor ingredient not contained in one of these regulations, and any non-flavor ingredient, shall be separately listed on the label.

(3) In cases where the flavor contains a solely natural flavor(s), the flavor shall be so labeled, e.g., "strawberry flavor," "banana flavor," or "natural strawberry flavor." In cases where the flavor contains both a natural flavor and an artificial flavor, the flavor shall be so labeled, e.g., "natural and artificial strawberry flavor." In cases where the flavor contains a solely artificial flavor(s), the flavor shall be so labeled, e.g., "artificial strawberry flavor."

(h) The label of a food to which flavor is added shall declare the flavor in the statement of ingredients in the following way:

(1) Spice, natural flavor, and artificial flavor may be declared as "spice," "natural flavor," or "artificial flavor," or any combination thereof, as the case may be.

(2) An incidental additive in a food, originating in a spice or flavor used in the manufacture of the food, need not be declared in the statement of ingredients if it meets the requirements of § 501.100(a)(3).

(3) Substances obtained by cutting, grinding, drying, pulping, or similar processing of tissues derived from fruit, vegetable, meat, fish, or poultry, e.g., powdered or granulated onions, garlic powder, and celery powder, are commonly understood by consumers to be food rather than flavor and shall be declared by their common or usual name.

(4) Any salt (sodium chloride) used as an ingredient in food shall be declared by its common or usual name "salt."

(5) Any monosodium glutamate used as an ingredient in food shall be declared by its common or usual name "monosodium glutamate."

(6) Any pyroligneous acid or other artificial smoke flavors used as an ingredient in a food may be declared as artificial flavor or artificial smoke flavor. No representation may be made, either directly or implied, that a food flavored with pyroligneous acid or other artificial smoke flavor has been smoked or has a true smoked

flavor, or that a seasoning sauce or similar product containing pyroligneous acid or other artificial smoke flavor and used to season or flavor other foods will result in a smoked product or one having a true smoked flavor.

(i) If the label, labeling, or advertising of a food makes any direct or indirect representations with respect to the primary recognizable flavor(s), by word, vignette, e.g., depiction of a fruit, or other means, or if for any other reason the manufacturer or distributor of a food wishes to designate the type of flavor in the food other than through the statement of ingredients, such flavor shall be considered the characterizing flavor and shall be declared in the following way:

(1) If the food contains no artificial flavor which simulates, resembles or reinforces the characterizing flavor, the name of the food on the principal display panel or panels of the label shall be accompanied by the common or usual name of the characterizing flavor in letters not less than one-half the height of the letters used in the name of the food, except that:

(i) If the food is one that is commonly expected to contain a characterizing food ingredient, and the food contains natural flavor derived from such ingredient and an amount of characterizing ingredient insufficient to independently characterize the food, or the food contains no such ingredient, the name of the characterizing flavor may be immediately preceded by the word "natural" and shall be immediately followed by the word "flavored" in letters not less than one-half the height of the letters in the name of the characterizing flavor.

(ii) If none of the natural flavor used in the food is derived from the product whose flavor is simulated, the food in which the flavor is used shall be labeled either with the flavor of the product from which the flavor is derived or as "artificially flavored."

(iii) If the food contains both a characterizing flavor from the product whose flavor is simulated and other natural flavor which simulates, resembles or reinforces the characterizing flavor, the food shall be labeled in accordance with the introductory text

and paragraph (1)(1)(i) of this section and the name of the food shall be immediately followed by the words "with other natural flavor" in letters not less than one-half the height of the letters used in the name of the characterizing flavor.

(2) If the food contains any artificial flavor which simulates, resembles or reinforces the characterizing flavor, the name of the food on the principal display panel or panels of the label shall be accompanied by the common or usual name(s) of the characterizing flavor, in letters not less than one-half the height of the letters used in the name of the food and the name of the characterizing flavor shall be accompanied by the word(s) "artificial" or "artificially flavored," in letters not less than one-half the height of the letters in the name of the characterizing flavor.

(3) Wherever the name of the characterizing flavor appears on the label (other than in the statement of ingredients) so conspicuously as to be easily seen under customary conditions of purchase, the words prescribed by this paragraph shall immediately and conspicuously precede or follow such name, without any intervening written, printed, or graphic matter, except:

(i) Where the characterizing flavor and a trademark or brand are presented together, other written, printed, or graphic matter that is a part of or is associated with the trademark or brand may intervene if the required words are in such relationship with the trademark or brand as to be clearly related to the characterizing flavor; and

(ii) If the finished product contains more than one flavor subject to the requirements of this paragraph, the statements required by this paragraph need appear only once in each statement of characterizing flavors present in such food.

(iii) If the finished product contains three or more distinguishable characterizing flavors, or a blend of flavors with no primary recognizable flavor, the flavor may be declared by an appropriately descriptive generic term in lieu of naming each flavor.

(4) A flavor supplier shall certify, in writing, that any flavor he supplies

which is designated as containing no artificial flavor does not, to the best of his knowledge and belief, contain any artificial flavor, and that he has added no artificial flavor to it. The requirement for such certification may be satisfied by a guarantee under section 303(c)(2) of the act which contains such a specific statement. A flavor used shall be required to make such a written certification only where he adds to or combines another flavor with a flavor which has been certified by a flavor supplier as containing no artificial flavor, but otherwise such user may rely upon the supplier's certification and need make no separate certification. All such certifications shall be retained by the certifying party throughout the period in which the flavor is supplied and for a minimum of 3 years thereafter, and shall be subject to the following conditions:

(i) The certifying party shall make such certifications available upon request at all reasonable hours to any duly authorized officer, or employee of the Food and Drug Administration or any other employee acting on behalf of the Secretary of Health and Human Services. Such certifications are regarded by the Food and Drug Administration as reports to the government and as guarantees or other undertakings within the meaning of section 301(h) of the act and subject the certifying party to the penalties for making any false report to the government under 18 U.S.C. 1001 and any false guarantee or undertaking under section 303(a) of the act. The defenses provided under section 303(c)(2) of the act shall be applicable to the certifications provided for in this section.

(ii) Wherever possible, the Food and Drug Administration shall verify the accuracy of a reasonable number of certifications made pursuant to this section, constituting a representative sample of such certifications, and shall not request all such certifications.

(iii) Where no person authorized to provide such information is reasonably available at the time of inspection, the certifying party shall arrange to have such person and the relevant materials and records ready for verification as soon as practicable; provided that, whenever the Food and Drug Adminis-

tration has reason to believe that the supplier or user may utilize this period to alter inventories or records, such additional time shall not be permitted. Where such additional time is provided, the Food and Drug Administration may require the certifying party to certify that relevant inventories have not been materially disturbed and relevant records have not been altered or concealed during such period.

(iv) The certifying party shall provide, to an officer or representative duly designated by the Secretary, such qualitative statement of the composition of the flavor or product covered by the certification as may be reasonably expected to enable the Secretary's representatives to determine which relevant raw and finished materials and flavor ingredient records are reasonably necessary to verify the certifications. The examination conducted by the Secretary's representative shall be limited to inspection and review of inventories and ingredient records for those certifications which are to be verified.

(v) Review of flavor ingredient records shall be limited to the qualitative formula and shall not include the quantitative formula. The person verifying the certifications may make only such notes as are necessary to enable him to verify such certification. Only such notes or such flavor ingredient records as are necessary to verify such certification or to show a potential or actual violation may be removed or transmitted, from the certifying party's place of business: *Provided*, That, where such removal or transmittal is necessary for such purposes the relevant records and notes shall be retained as separate documents in Food and Drug Administration files, shall not be copied in other reports, and shall not be disclosed publicly other than in a judicial proceeding brought pursuant to the act or 18 U.S.C. 1001.

(j) A food to which a chemical preservative(s) is added shall, except when exempt pursuant to § 501.100, bear a label declaration stating both the common or usual name of the ingredient(s) and a separate description of its function, e.g., "preservative," "to retard spoilage," "a mold in-

hibitor," "to help protect flavor" or "to promote color retention."

(Secs. 402, 403, 499, 701(a), 702, 703, 704, 52 Stat. 1046, 1047, 1048-1049 as amended, 1055, 1056-1057 as amended; 21 U.S.C. 342, 343, 348, 371(a), 372, 373, 374)

[41 FR 38619, Sept. 10, 1976, as amended at 42 FR 14091, Mar. 15, 1977; 42 FR 15675, Mar. 22, 1977]

Subparts C-E [Reserved]

Subpart F—Exemptions From Animal Food Labeling Requirements

§ 501.100 Animal food; exemptions from labeling.

(a) The following foods are exempt from compliance with the requirements of section 403(i)(2) of the act (requiring a declaration on the label of the common or usual name of each ingredient when the food is fabricated from two or more ingredients).

(1) An assortment of different items of food, when variations in the items that make up different packages packed from such assortment normally occur in good packing practice and when such variations result in variations in the ingredients in different packages, with respect to any ingredient that is not common to all packages. Such exemption, however, shall be on the condition that the label shall bear, in conjunction with the names of such ingredients as are common to all packages, a statement (in terms that are as informative as practicable and that are not misleading) indicating by name other ingredients which may be present.

(2) A food having been received in bulk containers at a retail establishment, if displayed to the purchaser with either (i) the labeling of the bulk container plainly in view or (ii) a counter card, sign, or other appropriate device bearing prominently and conspicuously the information required to be stated on the label pursuant to section 403(i)(2) of the act.

(3) Incidental additives that are present in a food at insignificant levels and do not have any technical or functional effect in that food. For the purposes of this paragraph (a)(3), incidental additives are:

(i) Substances that have no technical or functional effect but are present in a food by reason of having been incorporated into the food as an ingredient of another food, in which the substance did have a functional or technical effect.

(ii) Processing aids, which are as follows:

(a) Substances that are added to a food during the processing of such food but are removed in some manner from the food before it is packaged in its finished form.

(b) Substances that are added to a food during processing, are converted into constituents normally present in the food, and do not significantly increase the amount of the constituents naturally found in the food.

(c) Substances that are added to a food for their technical or functional effect in the processing but are present in the finished food at insignificant levels and do not have any technical or functional effect in that food.

(iii) Substances migrating to food from equipment or packaging or otherwise affecting food that are not food additives as defined in section 201(s) of the act; or if they are food additives as so defined, they are used in conformity with regulations established pursuant to section 409 of the act.

(b) A food repackaged in a retail establishment is exempt from the following provisions of the act if the conditions specified are met.

(1) Section 403(e)(1) of the act (requiring a statement on the label of the name and place of business, of the manufacturer, packer, or distributor).

(2) Section 403(g)(2) of the act (requiring the label of a food which purports to be or is represented as one for which a definition and standard of identity has been prescribed to bear the name of the food specified in the definition and standard and, insofar as may be required by the regulation establishing the standard the common names of the optional ingredients present in the food), if the food is displayed to the purchaser with its interstate labeling clearly in view, or with a counter card, sign, or other appropriate device bearing prominently and

conspicuously the information required by these provisions.

(3) Section 403(d)(1) of the act (requiring the label to bear the common or usual name of the food), if the food is displayed to the purchaser with its interstate labeling clearly in view, or with a counter card, sign, or other appropriate device bearing prominently and, conspicuously the common or usual name of the food, or if the common or usual name of the food is clearly revealed by its appearance.

(c) [Reserved]

(d) Except as provided by paragraphs (e) and (f) of this section, a shipment or other delivery of a food which is, in accordance with the practice of the trade, to be processed, labeled, or repacked in substantial quantity at an establishment other than that where originally processed or packed, shall be exempt, during the time of introduction into and movement in interstate commerce and the time of holding in such establishment, from compliance with the labeling requirements of section 403 (c), (e), (g), (h), (i), (j) and (k) of the act if:

(1) The person who introduced such shipment or delivery into interstate commerce is the operator of the establishment where such food is to be processed, labeled, or repacked; or

(2) In case such person is not such operator, such shipment or delivery is made to such establishment under a written agreement, signed by and containing the post office addresses of such person and such operator, and containing such specifications for the processing, labeling, or repacking, as the case may be, of such food in such establishment as will ensure, if such specifications are followed, that such food will not be adulterated or misbranded within the meaning of the act upon completion of such processing, labeling, or repacking. Such person and such operator shall each keep a copy of such agreement until 2 years after the final shipment or delivery of such food from such establishment, and shall make such copies available for inspection at any reasonable hour to any officer or employee of the Department who requests them.

(e) Conditions affecting expiration of exemptions.

(1) An exemption of a shipment or other delivery of a food under paragraph (d)(1) of this section shall, at the beginning of the act of removing such shipment or delivery, or any part thereof, from such establishment become void ab initio if the food comprising such shipment, delivery, or part is adulterated or misbranded within the meaning of the act when so removed.

(2) An exemption of a shipment or other delivery of a food under paragraph (d)(2) of this section shall become void ab initio with respect to the person who introduced such shipment or delivery into interstate commerce upon refusal by such person to make available for inspection a copy of the agreement, as required by paragraph (d)(2) of this section.

(3) An exemption of a shipment or other delivery of a food under paragraph (d)(2) of this section shall expire:

(i) At the beginning of the act of removing such shipment or delivery, or any part thereof, from such establishment if the food comprising such shipment, delivery, or part is adulterated or misbranded within the meaning of the act when so removed; or

(ii) Upon refusal by the operator of the establishment where such food is to be processed, labeled, or repacked, to make available for inspection a copy of the agreement as required by such paragraph.

(f) [Reserved]

(g) The label declaration of a harmless marker used to identify a particular manufacturer's product may result in unfair competition through revealing a trade secret. Exemption from the label declaration of such a marker is granted, therefore, provided that the following conditions are met:

(1) The person desiring to use the marker without label declaration of its presence has submitted to the Commissioner of Food and Drugs full information concerning the proposed usage and the reasons why he believes label declaration of the marker should be subject to this exemption; and

(2) The person requesting the exemption has received from the Commissioner of Food and Drugs a finding

that the marker is harmless and that the exemption has been granted.

§ 501.103 Petitions requesting exemptions from or special requirements for label declaration of ingredients.

The Commissioner of Food and Drugs, either on his own initiative or on behalf of any interested person who has submitted a petition pursuant to Part 10 of this chapter may issue a proposal to amend § 501.4 to specify the manner in which an ingredient(s) shall be declared, i.e., by specific or class name, or § 501.100 to exempt an ingredient(s) from the requirements for label declaration.

[41 FR 38619, Sept. 10, 1976, as amended at 42 FR 15675, Mar. 22, 1977]

§ 501.105 Declaration of net quantity of contents when exempt.

(a) The principal display panel of a food in package form shall bear a declaration of the net quantity of contents. This shall be expressed in the terms of weight, measure, numerical count, or a combination of numerical count and weight or measure. The statement shall be in terms of fluid measure if the food is liquid, or in terms of weight if the food is solid, semisolid, or viscous, or a mixture of solid and liquid; except that such statement may be in terms of dry measure if the food is a fresh fruit, fresh vegetable, or other dry commodity that is customarily sold by dry measure. If there is a firmly established general consumer usage and trade custom of declaring the contents of a liquid by weight, or a solid, semisolid, or viscous product by fluid measure, it may be used. Whenever the Commissioner determines that an existing practice of declaring net quantity of contents by weight, measure, numerical count, or a combination in the case of a specific packaged food does not facilitate value comparisons by consumers and offers opportunity for consumer confusion, he will by regulation designate the appropriate term or terms to be used for such commodity.

(b)(1) Statements of weight shall be in terms of avoirdupois pound and ounce.

(2) Statements of fluid measure shall be in terms of the U.S. gallon of 231 cubic inches and quart, pint, and fluid ounce subdivisions thereof, and shall:

(i) In the case of frozen food that is sold and consumed in a frozen state, express the volume at the frozen temperature.

(ii) In the case of refrigerated food that is sold in the refrigerated state, express the volume at 40°F (4°C).

(iii) In the case of other foods, express the volume at 68°F (20°C).

(3) Statements of dry measure shall be in terms of the U.S. bushel of 2,150.42 cubic inches and peck, dry quart, and dry pint subdivisions thereof.

(c) When the declaration of quantity of contents by numerical count does not give adequate information as to the quantity of food in the package, it shall be combined with such statement of weight, measure, or size of the individual units of the foods as will provide such information.

(d) The declaration may contain common or decimal fractions. A common fraction shall be in terms of halves, quarters, eighths, sixteenths, or thirty-seconds; except that if there exists a firmly established general consumer usage and trade custom of employing different common fractions in the net quantity declaration of a particular commodity, they may be employed. A common fraction shall be reduced to its lowest terms; a decimal fraction shall not be carried out to more than two places. A statement that includes small fractions of an ounce shall be deemed to permit smaller variations than one which does not include such fractions.

(e) The declaration shall be located on the principal display panel of the label, and with respect to packages bearing alternate principal panels it shall be duplicated on each principal display panel.

(f) The declaration shall appear as a distinct item on the principal display panel, shall be separated (by at least a space equal to the height of the lettering used in the declaration) from other printed label information appearing above or below the declaration and (by at least a space equal to twice

the width of the letter "N" of the style of type used in the quantity of contents statement) from other printed label information appearing to the left or right of the declaration. It shall not include any term qualifying a unit of weight, measure, or count (such as "jumbo quart" and "full gallon") that tends to exaggerate the amount of the food in the container. It shall be placed on the principal display panel within the bottom 30 percent of the area of the label panel in lines generally parallel to the base on which the package rests as it is designed to be displayed: *Provided*, That on packages having a principal display panel of 5 square inches or less, the requirement for placement within the bottom 30 percent of the area of the label panel shall not apply when the declaration of net quantity of contents meets the other requirements of this part.

(g) The declaration shall accurately reveal the quantity of food in the package exclusive of wrappers and other material packed therewith; provided that in the case of foods packed in containers designed to deliver the food under pressure, the declaration shall state the net quantity of the contents that will be expelled when the instructions for use as shown on the container are followed. The propellant is included in the net quantity declaration.

(h) The declaration shall appear in conspicuous and easily legible boldface print or type in distinct contrast (by typography, layout, color, embossing, or molding) to other matter on the package; except that a declaration of net quantity blown, embossed, or molded on a glass or plastic surface is permissible when all label information is so formed on the surface. Requirements of conspicuousness and legibility shall include the specifications that:

(1) The ratio of height to width (of the letter) shall not exceed a differential of 3 units to 1 unit (no more than 3 times as high as it is wide).

(2) Letter heights pertain to upper case or capital letters. When upper and lower case or all lower case letters are used, it is the lower case letter "o" or its equivalent that shall meet the minimum standards.

(3) When fractions are used, each component numeral shall meet one-half the minimum height standards.

(i) The declaration shall be in letters and numerals in a type size established in relationship to the area of the principal display panel of the package and shall be uniform for all packages of substantially the same size by complying with the following type specifications:

(1) Not less than $\frac{1}{16}$ inch in height on packages the principal display panel of which has an area of 5 square inches or less.

(2) Not less than $\frac{1}{8}$ inch in height on packages the principal display panel of which has an area of more than 5 but not more than 25 square inches.

(3) Not less than $\frac{3}{16}$ inch in height on packages the principal display panel of which has an area of more than 25 but not more than 100 square inches.

(4) Not less than $\frac{1}{4}$ inch in height on packages the principal display panel of which has an area of more than 100 square inches, except not less than $\frac{1}{2}$ inch in height if the area is more than 400 square inches.

Where the declaration is blown, embossed, or molded on a glass or plastic surface rather than by printing, typing, or coloring, the lettering sizes specified in paragraphs (i) (1) through (4) of this section shall be increased by $\frac{1}{16}$ of an inch.

(j) On packages containing less than 4 pounds or 1 gallon and labeled in terms of weight or fluid measure:

(1) The declaration shall be expressed both in ounces, with identification by weight or by liquid measure and, if applicable (1 pound or 1 pint or more) followed in parentheses by a declaration in pounds for weight units, with any remainder in terms of ounces or common or decimal fractions of the pound (see examples set forth in paragraphs (m) (1) and (2) of this section), or in the case of liquid measure, in the largest whole units (quarts, quarts and pints, or pints, as appropriate) with any remainder in terms of fluid ounces or common or decimal fractions of the pint or quart (see examples in paragraphs (m) (3) and (4) of this section).

(2) If the net quantity of contents declaration appears on a random pack-

age, that is a package which is one of a lot, shipment, or delivery of packages of the same consumer commodity with varying weights and with no fixed weight pattern, it may, when the net weight exceeds 1 pound, be expressed in terms of pounds and decimal fractions of the pound carried out to not more than two decimal places. When the net weight does not exceed 1 pound, the declaration on the random package may be in decimal fractions of the pound in lieu of ounces (see example in paragraph (m)(5) of this section).

(3) The declaration may appear in more than one line. The term "net weight" shall be used when stating the net quantity of contents in terms of weight. Use of the terms "net" or "net contents" in terms of fluid measure or numerical count is optional. It is sufficient to distinguish avoirdupois ounce from fluid ounce through association of terms; for example, "Net wt. 6 oz." or "6 oz. net wt." and "6 fl. oz." or "net contents 6 fl. oz."

(k) On packages containing 4 pounds or 1 gallon or more and labeled in terms of weight or fluid measure, the declaration shall be expressed in pounds for weight units with any remainder in terms of ounces or common or decimal fraction of the pound, or in the case of fluid measure, it shall be expressed in the largest whole unit (gallons followed by common or decimal fraction of a gallon or by the next smaller whole unit or units (quarts, or quarts and pints)) with any remainder in terms of fluid ounces or common or decimal fractions of the pint or quart (see paragraph (m)(6) of this section).

(l) [Reserved]

(m) Examples:

(1) A declaration of $1\frac{1}{2}$ pounds weight shall be expressed as "Net Wt. 24 oz. (1 lb. 8 oz.)," "Net Wt. 24 oz. (1½ lb.)," or "Net Wt. 24 oz. (1.5 lb.)."

(2) A declaration of $\frac{3}{4}$ pound avoirdupois weight shall be expressed as "Net Wt. 12 oz."

(3) A declaration of 1 quart liquid measure shall be expressed as "Net 32 fl. oz. (1 qt.)."

(4) A declaration of $1\frac{1}{4}$ quarts liquid measure shall be expressed as "Net contents 56 fluid ounces (1 quart $1\frac{1}{4}$).

pints)" or as "Net 56 fluid oz. (1 qt. 1 pt. 8 oz.)," but not in terms of quart and ounce such as "Net 56 fluid oz. (1 quart 24 ounces)".

(5) On a random package, declaration of $\frac{3}{4}$ pound avoirdupois may be expressed as "Net Wt. .75 lb."

(6) A declaration of $2\frac{1}{2}$ gallons liquid measure shall be expressed as "Net contents $2\frac{1}{2}$ gallons," "Net contents 2.5 gallons," or "Net contents 2 gallons 2 quarts" and not as "2 gallons 4 pints".

(n) For quantities, the following abbreviations and none other may be employed (periods and plural forms are optional):

weight wt.
ounce oz.
pound lb.
gallon gal.

pint pt.
quart qt.
fluid fl.

(o) Nothing in this section shall prohibit supplemental statements at locations other than the principal display panel(s) describing in nondeceptive terms the net quantity of contents; provided, that such supplemental statements of net quantity of contents shall not include any term qualifying a unit of weight, measure, or count that tends to exaggerate the amount of the food contained in the package; for example, "jumbo quart" and "full gallon". Dual or combination declarations of net quantity of contents as provided for in paragraphs (a), (c), and (i) of this section (for example, a combination of net weight plus numerical count, net contents plus dilution directions of a concentrate, etc.) are not regarded as supplemental net quantity statements and may be located on the principal display panel.

(p) A separate statement of the net quantity of contents in terms of the metric system is not regarded as a supplemental statement and an accurate statement of the net quantity of contents in terms of the metric system of weight or measure may also appear on the principal display panel or on other panels.

(q) The declaration of net quantity of contents shall express an accurate statement of the quantity of contents of the package. Reasonable variations caused by loss or gain of moisture

during the course of good distribution practice or by unavoidable deviations in good manufacturing practice will be recognized. Variations from stated quantity of contents shall not be unreasonably large.

(r) [Reserved]

(s) On a multiunit retail package, a statement of the quantity of contents shall appear on the outside of the package and shall include the number of individual units, the quantity of each individual unit, and, in parentheses, the total quantity of contents of the multiunit package in terms of avoirdupois or fluid ounces, except that such declaration of total quantity need not be followed by an additional parenthetical declaration in terms of the largest whole units and subdivisions thereof, as required by paragraph (j)(1) of this section. A multiunit retail package may thus be properly labeled: "6-16 oz. bottles—(96 fl. oz.)" or "3-16 oz. cans—(net wt. 48 oz.)". For the purposes of this section, "multiunit retail package" means a package containing two or more individually packaged units of the identical commodity and in the same quantity, intended to be sold as part of the multiunit retail package but capable of being individually sold in full compliance with all requirements of the regulations in this part. Open multiunit retail packages that do not obscure the number of units nor prevent examination of the labeling on each of the individual units are not subject to this paragraph if the labeling of each individual unit complies with the requirements of paragraphs (f) and (i) of this section.

(t) Where the declaration of net quantity of contents is in terms of net weight and/or drained weight or volume and does not accurately reflect the actual quantity of the contents or the product falls below the applicable standard of fill of container because of equipment malfunction or otherwise unintentional product variation, and the label conforms in all other respects to the requirements of this chapter (except the requirement that food falling below the applicable standard of fill of container shall bear the general statement of substandard fill specified in § 564.14(b) of this

chapter), the mislabeled food product, including any food product that fails to bear the general statement of standard fill specified in § 564.14(b) of this chapter, may be sold by the manufacturer or processor directly to institutions operated by Federal, State or local governments: *Provided, That:*

(1) The purchaser shall sign a statement at the time of sale stating that he is aware that the product is mislabeled to include acknowledgement of the nature and extent of the mislabeling, e.g., "Actual net weight may be as low as —% below labeled quantity" and that any subsequent distribution by him of said product except for his own institutional use is unlawful. This statement shall be kept on file at the principal place of business of the manufacturer or processor for 2 years subsequent to the date of shipment of the product and shall be available to the Food and Drug Administration upon request.

(2) The product shall be labeled on the outside of its shipping container with the statement(s):

(i) When the variation concerns net weight and/or drained weight or volume—"Product Mislabeled. Actual net weight (drained weight or volume where appropriate) may be as low as —% below labeled quantity. This Product Not for Retail Distribution", the blank to be filled in with the maximum percentage variance between the labeled and actual weight or volume of contents of the individual packages in the shipping container, and

(ii) When the variation is in regard to a fill of container standard—"Product Mislabeled. Actual fill may be as low as —% below standard of fill. This Product Not for Retail Distribution."

(3) The statements required by paragraphs (i)(2) (i) and (ii) of this section, which may be consolidated where appropriate, shall appear prominently and conspicuously as compared to other printed matter on the shipping container and in boldface print or type on a clear, contrasting background in order to render them likely to be read and understood by the purchaser under ordinary conditions of purchase.

(Sec. 5(a), 80 Stat. 1298; 15 U.S.C. 1454)

§ 501.110 Animal feed labeling: collective names for feed ingredients.

(a) An animal feed shall be exempt from the requirements of section 403(i)(2) of the act with respect to its label bearing the common or usual names of the animal feed ingredients listed in paragraph (b) of this section under the following prescribed conditions:

(1) The animal feed is intended solely for livestock and poultry.

(2) The label of the animal feed bears the collective name(s) prescribed in paragraph (b) of this section in lieu of the corresponding common or usual names of the individual feed ingredients contained therein.

(3) The label of the animal feed otherwise conforms to the requirements of section 403(i)(2) of the act.

(4) The ingredients of any feed listed in paragraph (b) of this section neither contain nor are food additives as defined in section 201(s) of the act unless provided for by and in conformity with applicable regulations established pursuant to section 409 of the act.

(b) Each collective name referred to in this paragraph may be used for the purpose of labeling where one or more of the ingredients listed for that collective name are present. The animal feed ingredients listed under each of the collective names are the products defined by the Association of American Feed Control Officials. The collective names are as follows:

(1) "Animal protein products" include one or more of the following: Animal products, marine products, and milk products.

(2) "Forage products" include one or more of the following: Alfalfa meals, entire plant meals, hays, and stem meals.

(3) "Grain products" include one or more of the following: Barley, grain sorghums, maize (corn), oats, rice, rye, and wheat.

(4) "Plant protein products" include one or more of the following: Algae meals, coconut meals (copra), cottonseed meals, guar meal, linseed meals, peanut meals, safflower meals, soybean meals, sunflower meals, and yeasts.

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(5) "Processed grain byproducts" include one or more of the following: Brans, brewers dried grains, distillers grains, distillers solubles, flours, germ meals, gluten feeds, gluten meals, grits, groats, hominy feeds, malt sprouts, middlings, pearled, polishings, shorts, and wheat mill run.

(6) "Roughage products" include one or more of the following: Cobs, hulls, husks, pulps, and straws.

PART 502—COMMON OR USUAL NAMES FOR NONSTANDARDIZED ANIMAL FOODS

Sec.

502.5 General principles.

502.19 Petitions.

§ 502.5 General principles.

(a) The common or usual name of a food, which may be a coined term, shall accurately identify or describe, in as simple and direct terms as possible, the basic nature of the food or its characterizing properties or ingredients. The name shall be uniform among all identical or similar products and may not be confusingly similar to the name of any other food that is not reasonably encompassed within the same name. Each class or subclass of food shall be given its own common or usual name that states, in clear terms, what it is in a way that distinguishes it from different foods.

(b) The common or usual name of a food shall include the percentage(s) of any characterizing ingredient(s) or component(s) when the proportion of such ingredient(s) or component(s) in the food has a material bearing on price or consumer acceptance or when the labeling or the appearance of the food may otherwise create an erroneous impression that such ingredient(s) or component(s) is present in an amount greater than is actually the case. The following requirements shall apply unless modified by a specific regulation in this part.

(1) The percentage of a characterizing ingredient or component shall be declared on the basis of its quantity in the finished product (i.e., weight/weight in the case of solids, or volume/volume in the case of liquids).

(2) The percentage of a characterizing ingredient or component shall be declared by the words "containing (or contains) — percent (or %) —" or "— percent (or %) —" with the first blank filled in with the percentage expressed as a whole number not greater than the actual percentage of the ingredient or component named and the second blank filled in with the common or usual name of the ingredient or component. The word "containing" (or "contains"), when used, shall appear on a line immediately below the part of the common or usual name of the food required by paragraph (a) of this section. For each characterizing ingredient or component, the words "— percent (or %) —" shall appear following or directly below the word "containing" (or "contains"), or directly below the part of the common or usual name of the food required by paragraph (a) of this section when the word "containing" (or "contains") is not used, in easily legible boldface print or type in distinct contrast to other printed or graphic matter, and in a height not less than the larger of the following alternatives:

(i) Not less than one-sixteenth inch in height on packages having a principal display panel with an area of 5 square inches or less and not less than one-eighth inch in height if the area of the principal display panel is greater than 5 square inches; or

(ii) Not less than one-half the height of the largest type appearing in the part of the common or usual name of the food required by paragraph (a) of this section.

(c) The common or usual name of a food shall include a statement of the presence or absence of any characterizing ingredient(s) or component(s) and/or the need for the user to add any characterizing ingredient(s) or component(s) when the presence or absence of such ingredient(s) or component(s) in the food has a material bearing on price or consumer acceptance or when the labeling or the appearance of the food may otherwise create an erroneous impression that such ingredient(s) or component(s) is present when it is not, and consumers may otherwise be misled about the presence or absence of the

ingredient(s) or component(s) in the food. The following requirements shall apply unless modified by a specific regulation in this part.

(1) The presence or absence of a characterizing ingredient or component shall be declared by the words "containing (or contains) _____" or "containing (or contains) no _____" or "no _____" or "does not contain _____," with the blank being filled in with the common or usual name of the ingredient or component.

(2) The need for the user of a food to add any characterizing ingredient(s) or component(s) shall be declared by an appropriate informative statement.

(3) The statement(s) required under paragraph (c) (1) and/or (2) of this section shall appear following or directly below the part of the common or usual name of the food required by paragraphs (a) and (b) of this section, in easily legible boldface print or type in distinct contrast to other printed or graphic matter, and in a height not less than the larger of the alternatives established under paragraph (b)(2) (i) and (ii) of this section.

(d) A common or usual name of a food may be established by common usage or by establishment of a regulation in this part, in a standard of identity, or in other regulations in this chapter.

(Secs. 201(n), 403, 701(a), 52 Stat. 1041 as amended, 1047-48 as amended, 1055 (21 U.S.C. 321(n), 343, 371(a)))

[41 FR 38627, Sept. 10, 1976. Redesignated at 42 FR 14091, Mar. 15, 1977]

§ 502.19 Petitions.

(a) The Commissioner of Food and Drugs, either on his own initiative or on behalf of any interested person who has submitted a petition, may publish a proposal to issue, amend, or revoke, under this part, a regulation prescribing a common or usual name for a food, pursuant to Part 10 of this chapter.

(b) If the principal display panel of a food for which a common or usual name regulation is established is too small to accommodate all mandatory requirements, the Commissioner may establish by regulation an acceptable alternative, e.g., a smaller type size. A petition requesting such a regulation,

which would amend the applicable regulation, shall be submitted pursuant to Part 10 of this chapter.

(Secs. 201(n), 403, 701(a), 52 Stat. 1041 as amended, 1047-48 as amended, 1055 (21 U.S.C. 321(n), 343, 371(a)))

[42 FR 4716, Jan. 25, 1977; 42 FR 10980, Feb. 25, 1977. Redesignated at 42 FR 14091, Mar. 15, 1977, and amended at 42 FR 15675, Mar. 22, 1977; 42 FR 24254, May 13, 1977]

PART 505—INTERPRETIVE STATEMENTS RE: WARNINGS ON ANIMAL DRUGS FOR OVER-THE-COUNTER SALE

Subpart A—Definitions and Interpretations

Sec.

505.3 Warnings on animal drugs intended for administration to diseased animals.

Subpart B—Required Warning and Caution Statements

505.10 Animal drug warning and caution statements required by regulations.

Subpart C—Voluntary Warning and Caution Statements

505.20 Recommended animal drug warning and caution statements.

AUTHORITY: Secs. 502, 503, 506, 507, 701, 52 Stat. 1050, as amended, 1052, as amended, 1055-1056, as amended, 52 Stat. 854; 55 Stat. 851; 59 Stat. 463, as amended (21 U.S.C. 352, 353, 356, 357, 371).

SOURCE: 40 FR 13805, Mar. 27, 1975, unless otherwise noted.

Subpart A—Definitions and Interpretations

§ 505.3 Warnings on animal drugs intended for administration to diseased animals.

None of the warning or caution statements recommended for use in the labeling of drugs intended for administration to diseased animals shall be construed to suggest or imply that any product of a diseased animal is suitable for food use. (See section 402(a)(5) of the act.)

§ 505.10

Subpart B—Required Warning and Caution Statements

§ 505.10 Animal drug warning and caution statements required by regulations.

ANIMAL FEED CONTAINING PENICILLIN, STREPTOMYCIN, DIHYDROSTREPTOMYCIN, CHLORTETRACYCLINE, TETRACYCLINE, CHLORAMPHENICOL, OR BACITRACIN, WITH OTHER DRUGS. (See § 510.515 of this chapter.)

A warning to the following effect is required when animal feeds containing any of the above-named antibiotics also contain the following drugs:

Arsanilic acid, sodium arsanilate, or 3-nitro-4-hydroxyphenol arsonic acid (3-nitro-4-hydroxyphenylarsonic acid) for poultry and swine. (See § 510.515 (a) and (b) of this chapter.)

Warning—Discontinue use 5 days before the treated animals are slaughtered for human consumption.

Chlortetracycline for leptospirosis of swine. (See § 510.515(b)(41) of this chapter.)

A warning to the following effect is required on preparations containing, per ton of feed, 400 grams of chlortetracycline:

Warning—Discontinue use 10 days before the treated animals are slaughtered for human consumption.

Hygromycin B for swine. (See § 510.515(b) of this chapter.)

Warning—Discontinue use 48 hours before the treated swine are slaughtered for human consumption.

Nystatin for turkeys. (See § 510.515(b) of this chapter.)

Warning—If used in laying hens, eggs are to be used for hatching purposes only.

ANTIBIOTIC-CONTAINING PREPARATIONS FOR VETERINARY USE. (See Parts 540, 544, 546, 548 and 555 of this chapter.)

All drugs containing penicillin, streptomycin, dihydrostreptomycin, chlortetracycline, tetracycline, chloramphenicol, or bacitracin or any of their derivatives, labeled solely for veterinary use and bearing directions for use by the laity, are required to bear a label statement to the effect "For veterinary use only."

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BACITRACIN-CONTAINING OINTMENTS. (See Part 548 of this chapter.)

All bacitracin-containing ointments are required to bear the label statements:

For use only in the prevention of infection in minor cuts and abrasions. Use of the drug should be discontinued and a veterinarian consulted if signs of infection or irritation appear.

BACITRACIN- (OR ZINC BACITRACIN-) POLYMYXIN OINTMENT; BACITRACIN - POLYMYXIN - NEO-MYCIN OINTMENT. (See §§ 448.510(c) and 448.510(e) of this chapter.)

These drugs are required to bear a label statement to the effect "For use only in the prevention of infection in minor cuts and abrasions. Use of the drug should be discontinued and a veterinarian consulted if signs of infection or irritation appear."

If they are in liquid form they also bear the statement: "Not for injection."

BACITRACIN OR FEED GRADE BACITRACIN POWDER ORAL VETERINARY; BACITRACIN METHYLENE DISALICYLATE AND STREPTOMYCIN SULFATE CAPSULES, POWDER, OR TABLETS ORAL VETERINARY. (See §§ 548.112(d)(a), 548.112(b)(a) of this chapter.)

These drugs are required to bear the label statement: "For oral veterinary use only."

CHLORAMPHENICOL OPHTHALMIC. (See § 555.310a of this chapter.)

Warning—Not for injection.

CHLORAMPHENICOL OTIC; CHLORAMPHENICOL TOPICAL. (See § 555.310(e) of this chapter.)

Warning—For external use only.

CHLORTETRACYCLINE OR TETRACYCLINE-CONTAINING PREPARATIONS FOR VETERINARY USE ONLY. (See Part 546 of this chapter.)

All drugs containing chlortetracycline or tetracycline or their derivatives, labeled solely for veterinary use and bearing directions for use by the laity, are required to bear a label statement to the effect "For veterinary use only."

CHLORTETRACYCLINE OR TETRACYCLINE-CONTAINING PREPARATIONS FOR OPHTHALMIC, OTIC, OR ORAL USE; CHLORTETRACYCLINE-OR TETRACYCLINE-CONTAINING PREPARATIONS WITH VASOCONSTRICTOR. (See §§ 546.180a(a), 546.180e(a), and 546.312b(a) of this chapter.)

Warning—Not for injection.

CHLORTETRACYCLINE ORAL VETERINARY (CRUDE); CHLORTETRACYCLINE SEED. (See §§ 546.110a(a) and 546.110b(a) of this chapter.)

These drugs are required to bear the label statement: "For oral veterinary use only."

TETRACYCLINE HYDROCHLORIDE FOR INTRAMUSCULAR USE. (See § 446.281b(a) of this chapter.)

This drug is required to bear the label statement: "For intramuscular use only."

BUFFERED CRYSTALLINE PENICILLIN. (See § 440.81(a) of this chapter.)

If represented for use as a treatment for mastitis, the statement: "Important—Milk from treated segments of udders should be discarded or used for purposes other than human consumption for at least 72 hours after the last treatment."

BUFFERED PENICILLIN POWDER, PENICILLIN POWDER WITH BUFFERED AQUEOUS DILUENT; DIBENZYLAMINE PENICILLIN AND POTASSIUM PENICILLIN POWDER, BUFFERED; PENICILLIN WITH VASOCONSTRICTOR. (See §§ 540.174a(a) and 540.160(a) of this chapter.)

Warning—Not for injection.

CRYSTALLINE PENICILLIN-STREPTOMYCIN (OR DIHYDRO-STREPTOMYCIN-) POLYMYXIN-OXYTETRACYCLINE-CARBOMYCIN POWDER VETERINARY. (See § 540.881(a) of this chapter.)

These drugs are required to bear the label statement: "For udder instillations of cattle only."

EPHEDRINE PENICILLIN TABLETS. (See § 540.163(a) of this chapter.)

Warning—Not for injection or oral use.

EPINEPHRINE INJECTION 1:1000 in 10-MILLILITER CONTAINERS FOR EMERGENCY TREATMENT OF ANAPHYLACTOID SHOCK IN CATTLE, HORSES, SHEEP, AND SWINE. (See § 500.65 of this chapter.)

The label for epinephrine injection 1:1000 packaged for over-the-counter sale for veterinary use must bear the following statements in a prominent and conspicuous manner: "For emergency use only in the treatment of anaphylactoid shock."

"Usual dosage: Cattle, horses, sheep, and swine—1 cubic centimeter per 100 pounds of body weight. Inject subcutaneously."

The labeling must also bear a description of the symptoms of anaphylactoid shock including glassy eyes, increased salivation, grinding of the teeth, rapid breathing, muscular tremors, staggering gait, and collapse with death following. These symptoms may appear shortly after injection of a bacteria, vaccine, or antibiotic.

PENICILLIN-CONTAINING PREPARATIONS FOR INTRAMUSCULAR USE ONLY. (See §§ 540.250(a), 540.253, 540.255c(a), 540.265a, 540.265b(a), 540.274a(a), 540.274f(a), 540.281a(a) of this chapter.)

All these preparations are required to bear the label statement: "For intramuscular use only."

PENICILLIN-CONTAINING OINTMENTS. (See Part 540 of this chapter.)

If these preparations are labeled solely for udder instillations of cattle and are packaged in glass containers, they are required to bear the label statements: "Not for injection. For udder instillations of cattle only."

PENICILLIN FOR SURFACE APPLICATION.

If the drug is not sterile, the statements: "Not sterile—Not for injection—Not to be used in deep wounds or body cavities."

PROCAINE PENICILLIN AND STREPTOMYCIN (OR DIHYDRO-STREPTOMYCIN) IN OIL; DIBENZYLAMINE PENICILLIN AND

STREPTOMYCIN (OR DIHYDROSTREPTOMYCIN) IN OIL; PROCAINE PENICILLIN-STREPTOMYCIN (OR DIHYDROSTREPTOMYCIN-) POLYMYXIN IN OIL (OR OINTMENT). (See §§ 540.274e(a) and 540.260(a) of this chapter.)

These drugs are required to bear the label statements: "For udder instillations of cattle only" or "For subcutaneous injection in fowl only. Inject in the neck immediately behind the head."

PROCAINE PENICILLIN IN OIL; PROCAINE PENICILLIN AND STREPTOMYCIN (OR DIHYDROSTREPTOMYCIN) IN OIL; PENICILLIN-STREPTOMYCIN (OR DIHYDROSTREPTOMYCIN-) NEOMYCIN IN OIL; BENZATHINE PENICILLIN G IN OIL; BENZATHINE PENICILLIN G-PROCAINE PENICILLIN G-STREPTOMYCIN (OR DIHYDROSTREPTOMYCIN) IN OIL. (See §§ 540.255b, 540.274c(a), and 540.274e(a) of this chapter.)

These drugs are required to bear the label statements:

"For udder instillations of cattle only" (if intended for such use); or

"For subcutaneous injection in fowl only. Inject in the neck immediately behind the head." (if packaged and labeled solely for subcutaneous injection in fowl).

STREPTOMYCIN FOR TOPICAL USE. (See § 544.370a of this chapter.)

Caution—Not for intravenous or systemic medication.

DISPENSERS PRESSURIZED BY GASEOUS PROPELLANTS FOR DRUGS

The label on each package of a drug in a self-pressurized container in which the propellant consists in whole or in part of a fully halogenated chlorofluoroalkane (chlorofluorocarbon) shall bear the following warning:

Warning—Contains a chlorofluorocarbon that may harm the public health and environment by reducing ozone in the upper atmosphere.

This required warning for self-pressurized containers that contain a fully halogenated chlorofluorocarbon shall appear on an appropriate panel with such prominence and conspicuousness

as to render it likely to be read and understood by ordinary individuals under normal conditions of purchase. The warning may appear on a firmly affixed tag, tape, card, or sticker or similar overlabeled attached to the package. The warning shall appear prominently and conspicuously as compared to other words, statements, designs, or devices and in bold type on contrasting background, but in no case may the letters be less than 1/16 inch in height.

The warning is required only on a self-pressurized container that uses a chlorofluorocarbon in whole or in part as a propellant to expel from the container liquid or solid material different from the propellant.

(Secs. 201(n), 301, 402, 403, 501, 502, 505, 507, 512, 601, 602, 701(a), 52 Stat. 1041-1043 as amended, 1046-1048 as amended, 1049, 1051-1053 as amended, 1054-1055, 57 Stat. 463 as amended, 82 Stat. 343-351 (21 U.S.C. 321(n), 331, 342, 343, 351, 352, 355, 357, 360b, 361, 362, and 371(a)); sec. 102(2), 83 Stat. 853 (42 U.S.C. 4332); 21 CFR 5.1)

(40 FR 13805, Mar. 27, 1975, as amended at 41 FR 10886, 11011, Mar. 15, 1976; 41 FR 38768, Sept. 13, 1976; 42 FR 22033, Apr. 29, 1977; 44 FR 22053, Apr. 13, 1979; 47 FR 51563, Nov. 16, 1982)

Subpart C—Voluntary Warning and Caution Statements

§ 505.20 Recommended animal drug warning and caution statements.

ACETYLAMINONITROTHIAZOLE FOR POULTRY.

Warning—Discontinue use at least 1 week before slaughtering birds for food to eliminate the drug from the food.

AMINONITROTHIAZOLE (2-AMINO-5-NITROTHIAZOLE) FOR POULTRY.

Warning—Discontinue use at least 1 week before slaughtering birds for food to eliminate the drug from the food.

ANESTHETICS FOR EXTERNAL USE (LOCAL ANESTHETICS).

Caution—Not for prolonged use. If the condition for which this preparation is used persists or if a rash or irritation develops, discontinue use and consult veterinarian.

ANTHELMINTICS.

Caution—Consult veterinarian before using in severely debilitated animals.

ANTHELMINTICS: PHENOTHIAZINE.

Warning—Do not treat lactating dairy animals.

Caution—Consult veterinarian before using in severely debilitated animals. Individual animals are occasionally sensitive to phenothiazine.

ANTIHISTAMINICS FOR EXTERNAL USE.

Caution—If the condition for which this preparation is used persists or if a rash or irritation develops, discontinue use and consult veterinarian.

ANTISEPTICS FOR EXTERNAL USE.

Caution—In case of deep or puncture wounds or serious burns consult veterinarian. If redness, irritation, or swelling persists or increases, discontinue use and consult veterinarian.

CARBOLIC ACID (PHENOL) PREPARATIONS (MORE THAN 0.5 PERCENT) FOR EXTERNAL USE.

Caution—Use only as directed. Avoid contact with the eyes and mucous membranes. Do not apply to large areas of broken skin. Do not use on cats.

CORTISONE, HYDROCORTISONE, PREDNISOLONE AND PREDNISONE PREPARATIONS FOR EXTERNAL USE.

Caution—Do not use where infection (pus) is present, since the drug may allow infection to spread. If redness, irritation, or swelling persists or increases, discontinue use and consult veterinarian.

COUNTERIRRITANTS AND RUBEFACIENTS.

Caution—Do not apply to irritated skin or if excessive irritation develops. Avoid getting into eyes or on mucous membranes.

CREOSOTE, CRESOLS, GUAIACOL, AND SIMILAR SUBSTANCES IN PREPARATIONS FOR EXTERNAL USE.

Caution—Use only as directed. Avoid contact with the eyes and mucous membranes. Do not apply to large areas of broken skin. Not recommended for use on cats.

DIARRHEA PREPARATIONS.

Caution—If symptoms persist after using this preparation for 2 or 3 days, consult veterinarian.

DISPENSERS PRESSURIZED BY GASEOUS PROPELLANT FOR DRUGS FOR EXTERNAL USE.

Caution—Keep away from eyes or other mucous membranes. Avoid inhaling.

This warning is not necessary for preparations especially designed for use on mucous membranes.

Warning—Contents under pressure. Do not puncture. Do not use or store near heat or open flame. Exposure to temperatures above 130° Fahrenheit may cause bursting. Never throw container into fire or incinerator.

DRESSINGS, PROTECTIVE SPRAY-ON TYPE.

Caution—In case of deep or puncture wounds or serious burns or if redness, irritation, or swelling persists or increases, consult veterinarian.

Keep away from eyes or other mucous membranes. Avoid inhaling.

See also Dispensers Pressurized by Gaseous Propellant . . . for additional warnings to be included for products under pressure.

ESTROGEN PELLETS IN CATTLE AND SHEEP.

Warning—Implant pellets in _____ (name of the anatomical area) only. Any other location may result in violation of Federal law. Do not attempt salvage of implanted site for human or animal food.

NICARBAZIN FOR POULTRY.

Warning—Do not feed to laying hens in production. Discontinue use at least 4 days before slaughtering birds for food to eliminate the drug from the food.

OPHTHALMIC PREPARATIONS.

Caution—If condition persists or increases discontinue use and consult veterinarian. Keep container tightly closed.

Solutions should also include the following statement: "Do not touch applicator tip to any surface, since this may contaminate solution."

SALMONELLOSIS TREATMENTS FOR POULTRY.

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Important—Poultry that have survived salmonella outbreaks should not be kept for laying-house replacements or breeders, unless tests show that they are not carriers.

SULFONAMIDE PREPARATIONS (SYSTEMIC).

Caution—If symptoms persist after using this preparation for 2 or 3 days, consult veterinarian.

SULFONAMIDES FOR EXTERNAL USE.

Caution—If redness, irritation, or swelling persists or increases, discontinue use and consult veterinarian.

If the preparation has not been sterilized, the following statement should also be used.

Caution—This preparation has not been sterilized. Do not use in body cavities or deep wounds.

(Secs. 512, 701(a), 52 Stat. 1055, 82 Stat. 343-351 (21 U.S.C. 360b, 371(a))

[40 FR 13805, Mar. 27, 1975, as amended at 47 FR 51563, Nov. 14, 1982]

PART 507—THERMALLY PROCESSED LOW-ACID FOODS PACKAGED IN HERMETICALLY SEALED CONTAINERS

Subpart A—General Provisions

Sec.

507.3 Definitions.

507.5 Current good manufacturing practice.

507.10 Personnel.

Subpart B—[Reserved]

Subpart C—Equipment

507.40 Equipment and procedures.

Subpart D—Control of Components, Food Product Containers, Closures, and In-Process Materials

507.60 Containers.

Subpart E—Production and Process Controls

507.81 Product preparation.

507.83 Establishing scheduled processes.

507.87 Operations in the thermal processing room.

507.89 Deviations in processing, venting, or control of critical factors.

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Subpart F—Records and Reports

507.100 Processing and production records.

AUTHORITY: Secs. 402(a) (3) and (4), 701(a), 52 Stat. 1046, 1055 (21 U.S.C. 342(a) (3) and (4), 371(a)).

SOURCE: 44 FR 48598, Aug. 17, 1979, unless otherwise noted.

Subpart A—General Provisions

§ 507.3 Definitions.

For the purposes of this part, the following definitions apply:

(a) "Aseptic processing and packaging" means the filling of a commercially sterilized cooled product into presterilized containers, followed by aseptic hermetical sealing, with a presterilized closure, in an atmosphere free of microorganisms.

(b) "Bleeders" mean openings used to remove air that enters with steam from retorts and steam chambers and to promote circulation of steam in such retorts and steam chambers. Bleeders may serve as a means of removing condensate.

(c) "Come-up-time" means the time which elapses between the introduction of steam into the closed retort and the time when the retort reaches the required processing temperature.

(d) "Commercial processor" includes any person engaged in commercial, custom, or institutional (church, school, penal, or other organization) processing of food, including pet food. Persons engaged in the production of foods that are to be used in market or consumer tests are also included.

(e) "Commercial sterility": (1) "Commercial sterility" of thermally processed food means the condition achieved—

(i) By the application of heat which renders the food free of—

(a) Microorganisms capable of reproducing in the food under normal non-refrigerated conditions of storage and distribution; and

(b) Viable microorganisms (including spores) of public health significance; or

(ii) By the control of water activity and the application of heat, which renders the food free of microorganisms capable of reproducing in the

food under normal nonrefrigerated conditions of storage and distribution.

(2) "Commercial sterility" of equipment and containers used for aseptic processing and packaging of food means the condition achieved by application of heat, chemical sterilant(s), or other appropriate treatment that renders the equipment and containers free of viable microorganisms having public health significance, as well as microorganisms of nonhealth significance, capable of reproducing in the food under normal nonrefrigerated conditions of storage and distribution.

(f) "Critical factor" means any property, characteristic, condition, aspect, or other parameter, variation of which may affect the scheduled process and the attainment of commercial sterility.

(g) "Flame sterilizer" means an apparatus in which hermetically sealed containers are agitated at atmospheric pressure, by either continuous, discontinuous, or reciprocating movement, with impinging gas flames to achieve sterilization temperatures. A holding period in a heated section may follow the initial heating period.

(h) "Headspace, gross" is the vertical distance between the level of the product (generally the liquid surface) in an upright rigid container and the top edge of the container (the top of the double seam of a can or the top edge of a glass jar).

(i) "Headspace, net" of a container is the vertical distance between the level of the product (generally the liquid surface) in the upright rigid container and the inside surface of the lid.

(j) "Hermetically sealed container" means a container that is designed and intended to be secure against the entry of microorganisms and thereby to maintain the commercial sterility of its contents after processing.

(k) "Incubation" means the holding of a sample(s) at a specified temperature for a specified period of time for the purpose of permitting or stimulating the growth of microorganisms.

(l) "Initial temperature" means the average temperature of the contents of the coldest container to be processed at the time the thermal processing cycle begins, as determined after thorough stirring or shaking of the filled and sealed container.

(m) "Lot" means that amount of a product produced during a period of time indicated by a specific code.

(n) "Low-acid foods" means any foods, other than alcoholic beverages, with a finished equilibrium pH greater than 4.6 and a water activity (a_w) greater than 0.85. Tomatoes and tomato products having a finished equilibrium pH less than 4.7 are not classed as low-acid foods.

(o) "Minimum thermal process" means the application of heat to food, either before or after sealing in a hermetically sealed container, for a period of time and at a temperature scientifically determined to be adequate to ensure destruction of microorganisms of public health significance.

(p) "Operating process" means the process selected by the processor that equals or exceeds the minimum requirements set forth in the scheduled process.

(q) "Retort" means any closed vessel or other equipment used for the thermal processing of foods.

(r) "Scheduled process" means the process selected by the processor as adequate under the conditions of manufacture for a given product to achieve commercial sterility. This process may be in excess of that necessary to ensure destruction of microorganisms of public health significance, and shall be at least equivalent to the process established by a competent processing authority to achieve commercial sterility.

(s) "Shall" is used to state mandatory requirements.

(t) "Should" is used to state recommended or advisory procedures or to identify recommended equipment.

(u) "Vacuum-packed products" means those products that are sealed in a container under the vacuum specified in the scheduled process, the maintenance of which vacuum is critical to the adequacy of the scheduled process.

(v) "Vents" means openings through the retort shell, controlled by gate, plug cock, or other adequate valves used for the elimination of air during the venting period.

(w) "Water activity" (a_w) is a measure of the free moisture in a product and is the quotient of the water vapor

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pressure of the substance divided by the vapor pressure of pure water at the same temperature.

§ 507.5 Current good manufacturing practice.

The criteria in §§ 507.10, 507.40, 507.60, 507.81, 507.83, 507.87, 507.89, and 507.100 shall apply in determining whether the facilities, methods, practices, and controls used by the commercial processor in the manufacture, processing, or packing of low-acid foods in hermetically sealed containers are operated or administered in a manner adequate to protect the public health.

§ 507.10 Personnel.

The operators of processing systems, retorts, aseptic processing and packaging systems and product formulating systems (including systems wherein water activity is used in conjunction with thermal processing) and container closure inspectors shall be under the operating supervision of a person who has attended a school approved by the Commissioner for giving instruction appropriate to the preservation technology involved and who has been identified by that school as having satisfactorily completed the prescribed course of instruction. This person shall supervise only in those areas for which a school approved by the Commissioner identifies the person as having satisfactorily completed training.

Subpart B—[Reserved]

Subpart C—Equipment

§ 507.40 Equipment and procedures.

(a) *Equipment and procedures for pressure processing in steam in still retorts*—(1) *Indicating mercury-in-glass thermometer*. Each retort shall be equipped with at least one mercury-in-glass thermometer whose divisions are easily readable to 1° F and whose temperature range does not exceed 17° F per inch of graduated scale. Thermometers shall be tested for accuracy against a known accurate standard thermometer upon installation and at least once a year thereafter, or more

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frequently if necessary, to ensure their accuracy. Records of thermometer accuracy checks that specify date, standard used, method used, and person performing the test should be maintained. Each thermometer should have a tag, seal, or other means of identity that includes the date on which it was last tested for accuracy. A thermometer that has a divided mercury column or that cannot be adjusted to the standard shall be repaired or replaced before further use of the retort. Thermometers shall be installed where they can be accurately and easily read. Bulbs of indicating thermometers shall be installed either within the retort shell or in external wells attached to the retort. External wells or pipes shall be connected to the retort through at least a 3/4-inch diameter opening and equipped with a 1/2-inch or larger bleeder opening so located as to provide a full flow of steam past the length of the thermometer bulb. The bleeders for external wells shall emit steam continuously during the entire processing period. The mercury thermometer—not the recorder chart—shall be the reference instrument for indicating the processing temperature.

(2) *Temperature-recording device*. Each still retort shall have an accurate temperature-recording device. Graduations on the temperature-recording devices shall not exceed 2° F within a range of 10° F of the processing temperature. Each chart shall have a working scale of not more than 55° F per inch within a range of 20° F of the processing temperature. The temperature chart shall be adjusted to agree as nearly as possible with, but to be in no event higher than, the known accurate mercury-in-glass thermometer during the process time. A means of preventing unauthorized changes in adjustment shall be provided. A lock, or a notice from management posted at or near the recording device which provides a warning that only authorized persons are permitted to make adjustments, is a satisfactory means for preventing unauthorized changes. The recorder may be combined with the steam controller and may be a recording-controlling instrument. The temperature-recorder bulb shall be in-

stalled either within the retort shell or in a well attached to the shell. Each temperature-recorder bulb well shall have a $\frac{1}{8}$ -inch or larger bleeder which emits steam continuously during the processing period. Air-operated temperature controllers should have adequate filter systems to ensure a supply of clean, dry air.

(3) *Pressure gages.* Each retort should be equipped with a pressure gage that should be graduated in divisions of 2 pounds or less.

(4) *Steam controller.* Each retort shall be equipped with an automatic steam controller to maintain the retort temperature. This may be a recording-controlling instrument when combined with a recording thermometer. The steam controller may be air-operated and actuated by a temperature sensor positioned near the mercury-in-glass thermometer in the retort; a steam controller activated by the steam pressure of the retort is acceptable if it is carefully maintained mechanically so that it operates satisfactorily.

(5) *Steam inlet.* The steam inlet to each still retort shall be large enough to provide sufficient steam for proper operation of the retort. Steam may enter either the top portion or the bottom portion of the retort but, in any case, shall enter the portion of the retort opposite the vent; for example, steam inlet in bottom portion and vent in top portion.

(6) *Crate supports.* A bottom crate support shall be used in vertical still retorts. Baffle plates shall not be used in the bottom of still retorts.

(7) *Steam spreaders.* Steam spreaders are continuations of the steam inlet line inside the retort. Horizontal still retorts shall be equipped with steam spreaders that extend the length of the retort. For steam spreaders along the bottom of the retort, the perforations should be along the top 90° of this pipe, that is, within 45° on either side of the top center. Horizontal still retorts over 30 feet long should have two steam inlets connected to the spreader. In vertical still retorts, the steam spreaders, if used, should be perforated along the center line of the pipe facing the interior of the retort or along the sides of the

pipe. The number of perforations should be such that the total cross-sectional area of the perforations is equal to $1\frac{1}{2}$ to 2 times the cross-sectional area of the smaller restriction in the steam inlet line.

(8) *Bleeders.* Bleeders, except those for thermometer wells, shall be one-eighth inch or larger and shall be wide open during the entire process, including the come-up-time. For horizontal still retorts, bleeders shall be located within approximately 1 foot of the outermost locations of containers at each end along the top of the retort; additional bleeders shall be located not more than 8 feet apart along the top. Bleeders may be installed at positions other than those specified above, as long as there is evidence in the form of heat distribution data that they accomplish adequate removal of air and circulation of steam within the retort. Vertical retorts shall have at least one bleeder opening located in that portion of the retort opposite the steam inlet. In retorts having top steam inlet and bottom venting, a bleeder shall be installed in the bottom of the retort to remove condensate. All bleeders shall be arranged so that the operator can observe that they are functioning properly.

(9) *Stacking equipment and position of containers.* Crates, trays, gondolas, etc., for holding containers shall be made of strap iron, adequately perforated sheet metal, or other suitable material. When perforated sheet metal is used for the bottoms, the perforations should be approximately the equivalent of 1-inch holes on 2-inch centers. If dividers are used between the layers of containers, they should be perforated as above. The positioning of containers in the retort, when specified in the scheduled process, shall be in accordance with that process.

(10) *Air valves.* Retorts using air for pressure cooling shall be equipped with a suitable valve to prevent air leakage into the retort during processing.

(11) *Water valves.* Retorts using water for cooling shall be equipped with a suitable valve to prevent leakage of water into the retort during processing.

(12) *Vents.* Vents shall be installed in such a way that air is removed from the retort before timing of the process is started. Vents shall be controlled by gate, plug cock, or other adequate type valves which shall be fully open to permit rapid discharge of air from the retort during the venting period. Vents shall not be connected directly to a closed drain system. If the overflow is used as a vent, there shall be an atmospheric break in the line before it connects to a closed drain. The vent shall be located in that portion of the retort opposite the steam inlet; for example, steam inlet in bottom portion and vent in top portion. Where a retort manifold connects several vent pipes from a single still retort, it shall be controlled by a gate, plug cock, or other adequate type valve. The retort manifold shall be of a size that the cross-sectional area of the pipe is larger than the total cross-sectional area of all connecting vents. The discharge shall not be directly connected to a closed drain without an atmospheric break in the line. A manifold header connecting vents or manifolds from several still retorts shall lead to the atmosphere. The manifold header shall not be controlled by a valve and shall be of a size that the cross-sectional area is at least equal to the total cross-sectional area of all connecting retort manifold pipes from all retorts venting simultaneously. Timing of the process shall not begin until the retort has been properly vented and the processing temperature has been reached. Some typical installations and operating procedures reflecting the requirements of this section for venting still retorts are given in paragraphs (a)(12) (i)(a) through (d) and (ii)(a) and (b) of this section.

(i) *Venting horizontal retorts.* (a) Venting through multiple 1-inch vents discharging directly to atmosphere.

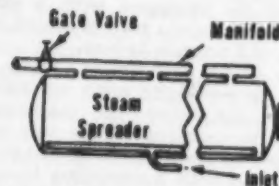


Specifications. One 1-inch vent for every 5 feet of retort length, equipped with a gate

or plug cock valve and discharging to atmosphere; end vents not more than 2½ feet from ends of retort.

Venting method. Vent valves should be wide open for at least 5 minutes and to at least 225° F, or at least 7 minutes and to at least 220° F.

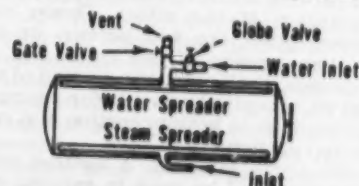
(b) Venting through multiple 1-inch vents discharging through a manifold to atmosphere.



Specifications. One 1-inch vent for every 5 feet of retort length; and vents not over 2½ feet from ends of retort; Size of manifold—for retorts less than 15 feet in length, 2½ inches; for retorts 15 feet and over in length, 3 inches.

Venting method. Manifold vent gate or plug cock valve should be wide open for at least 6 minutes and to at least 225° F, or for at least 8 minutes and to at least 220° F.

(c) Venting through water spreaders.

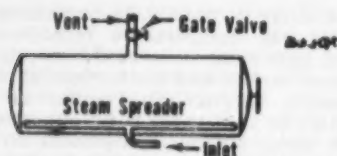


Size of vent and vent valve. For retorts less than 15 feet in length, 2 inches; for retorts 15 feet and over in length, 2½ inches.

Size of water spreader. For retorts less than 15 feet in length, 1½ inches; for retorts 15 feet and over in length, 2 inches. The number of holes should be such that their total cross-sectional area is approximately equal to the cross-sectional area of the vent pipe inlet.

Venting method. Water spreader vent gate or plug cock valve should be wide open for at least 5 minutes and to at least 225° F, or for at least 7 minutes and to at least 220° F.

(d) Venting through a single 2½-inch top vent (for retorts not exceeding 15 feet in length).



Specifications: A 2½-inch vent equipped with a 2½-inch gate or plug cock valve and located within 2 feet of the center of the retort.

Venting method: Vent gate or plug cock valve should be wide open for at least 4 minutes and to at least 220° F.

(ii) **Venting vertical retorts.** (a) Venting through a 1½-inch overflow.



Specifications. A 1½-inch overflow pipe equipped with a 1½-inch gate or plug cock valve and with not more than 6 feet of 1½-inch pipe beyond the valve before break to the atmosphere or to a manifold header.

Venting method. Vent gate or plug cock valve should be wide open for at least 4 minutes and to at least 218° F, or for at least 5 minutes and to at least 215° F.

(b) Venting through a single 1-inch side or top vent.



Specifications. A 1-inch vent in lid or top side, equipped with a 1-inch gate or plug cock valve and discharging directly into the atmosphere or to a manifold header.

Venting method. Vent gate or plug cock valve should be wide open for at least 5 minutes and to at least 230° F, or for at least 7 minutes and to at least 220° F.

(iii) Other installations and operating procedures that deviate from the above specifications may be used if there is evidence in the form of heat distribution data, which shall be kept on file, that they accomplish adequate venting of air.

(13) **Critical factors.** Critical factors specified in the scheduled process shall be measured and recorded on the processing record at intervals of sufficient frequency to ensure that the factors are within the limits specified in the scheduled process.

(i) When maximum fill-in or drained weight is specified in the scheduled process, it shall be measured and recorded at intervals of sufficient frequency to ensure that the weight of the product does not exceed the maximum for the given container size specified in the scheduled process.

(ii) Closing machine vacuum in vacuum-packed products shall be observed and recorded at intervals of sufficient frequency to ensure that the vacuum is as specified in the scheduled process.

(iii) Such measurements and recordings should be made at intervals not to exceed 15 minutes.

(iv) When the product style results in stratification or layering of the primary product in the containers, the positioning of containers in the retort shall be according to the scheduled process.

(b) **Equipment and procedures for pressure processing in water in still retorts—**(1) *Indicating mercury-in-glass thermometer.* Each retort shall be equipped with at least one mercury-in-glass thermometer whose divisions are easily readable to 1° F and whose temperature range does not exceed 17° F per inch of graduated scale. Thermometers shall be tested for accuracy against a known accurate standard thermometer upon installation and at least once a year thereafter, or more frequently if necessary, to ensure their accuracy. Records of thermometer accuracy checks which specify date, standard used, method used, and person performing the test should be maintained. Each thermometer should have a tag, seal, or other means of identity that includes the date when it was last tested for accuracy. A ther-

momometer that has a divided mercury column or that cannot be adjusted to the standard shall be repaired or replaced before further use of the retort. Thermometers shall be installed where they can be accurately and easily read. Bulbs of indicating thermometers shall be located in such a position that they are beneath the surface of the water throughout the process. On horizontal retorts, this entry should be made in the side at the center, and the thermometer bulbs shall be inserted directly into the retort shell. In both vertical and horizontal retorts, the thermometer bulbs shall extend directly into the water a minimum of at least 2 inches without a separable well or sleeve. The mercury thermometer—not the recorder chart—shall be the reference instrument for indicating the processing temperature.

(2) *Temperature-recording device.* Each still retort shall have an accurate temperature-recording device. Graduations on the temperature-recording devices shall not exceed 2° F within a range of 10° F of the processing temperature. Each chart shall have a working scale of not more than 55° F per inch within a range of 20° F of the processing temperature. The temperature chart shall be adjusted to agree as nearly as possible with, but to be in no event higher than, the known accurate mercury-in-glass thermometer during the process time. A means of preventing unauthorized changes in adjustment shall be provided. A lock, or a notice from management posted at or near the recording device which provides a warning that only, authorized persons are permitted to make adjustments, is a satisfactory means for preventing unauthorized changes. The recorder may be combined with the steam controller and may be a recording-controlling instrument. The recording-thermometer bulb should be located adjacent to the bulb of the mercury-in-glass thermometer, except in the case of a vertical retort equipped with a combination recorder-controller. In such vertical retorts, the temperature recorder-control bulb shall be located at the bottom of the retort below the lowest crate rest in such a position that the steam does

not strike it directly. In horizontal retorts, the temperature recorder-control bulb shall be located between the water surface and the horizontal plane passing through the center of the retort so that there is no opportunity for direct steam impingement on the control bulb. Air-operated temperature controllers should have adequate filter systems to ensure a supply of clean, dry air.

(3) *Pressure gages.* (i) Each retort should be equipped with a pressure gage, which should be graduated in divisions of 2 pounds or less.

(ii) Each retort should have an adjustable pressure relief or control valve of a capacity sufficient to prevent an undesired increase in retort pressure when the water valve is wide open and should be installed in the overflow line.

(4) *Steam controller.* Each retort shall be equipped with an automatic steam controller to maintain the retort temperature. This may be a recording-controlling instrument when combined with a recording thermometer.

(5) *Steam introduction.* Steam shall be distributed in the bottom of the retort in a manner adequate to provide uniform heat distribution throughout the retort. In vertical retorts, uniform steam distribution can be achieved by any of several methods. In horizontal retorts, the steam distributor shall run the length of the bottom of the retort with perforations distributed uniformly along the upper part of the pipe.

(6) *Crate supports.* A bottom crate support shall be used in vertical still retorts. Baffle plates shall not be used in the bottom of the retort. Centering guides should be installed so as to ensure that there is about a 1½-inch clearance between the side wall of the crate and the retort wall.

(7) *Stacking equipment and position of containers.* Crates, trays, gondolas, etc., for holding containers shall be made of strap iron, adequately perforated sheet metal, or other suitable material. When perforated sheet metal is used for the bottoms, the perforations should be approximately the equivalent of 1-inch holes on 2-inch centers. If divider plates are used between the layers of containers, they

should be perforated as above. The positioning of containers in the retort, when specified in the scheduled process, shall be in accordance with that process. Divider racks, trays, or other means of positioning of flexible containers shall be designed and employed to ensure even circulation of heating medium around all containers in the retort.

(8) *Drain valve.* A nonclogging, water-tight valve shall be used. Screens should be installed over all drain openings.

(9) *Water level indicator.* There shall be a means of determining the water level in the retort during operation, e.g., by using a gage, water glass, or petcock(s). Water shall cover the top layer of containers during the entire come-up-time and processing periods and should cover the top layer of containers during the cooling periods. The operator shall check and record the water level at intervals sufficient to ensure its adequacy.

(10)(i) *Air supply and controls.* In both horizontal and vertical still retorts for pressure processing in water, a means shall be provided for introducing compressed air at the proper pressure and rate. The proper pressure shall be controlled by an automatic pressure control unit. A check valve shall be provided in the air supply line to prevent water from entering the system. Air or water circulation shall be maintained continuously during the come-up-time and during processing and cooling periods; the adequacy of the air or water circulation for uniform heat distribution within the retort shall be established in accordance with procedures recognized by a competent processing authority and records shall be kept on file; if air is used to promote circulation, it shall be introduced into the steam line at a point between the retort and the steam control valve at the bottom of the retort.

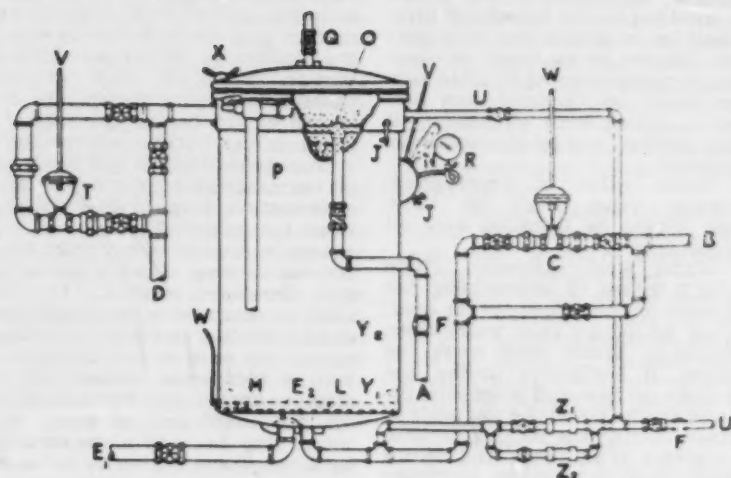
(ii) *Water circulation.* When a water circulating system is used for heat distribution, it shall be installed in such a manner that water will be drawn from the bottom of the retort through a suction manifold and discharged through a spreader which extends the length of the top of the retort. The holes in the water spreader shall be uniformly distributed and should have an aggregate area not greater than the cross-section area of the outlet line from the pump. The suction outlets should be protected with nonclogging screens to keep debris from entering the circulating system. The pump shall be equipped with a pilot light or other signaling device to warn the operator when it is not running, and with a bleeder to remove air when starting operations. Alternative methods for circulation of water in the retort may be used when established by a competent authority as adequate for even heat distribution.

(11) *Cooling water supply.* In vertical retorts the cooling water should be introduced at the top of the retort between the water and container levels; in horizontal retorts the cooling water should be introduced into the suction side of the pump. A check valve should be included in the cooling water line.

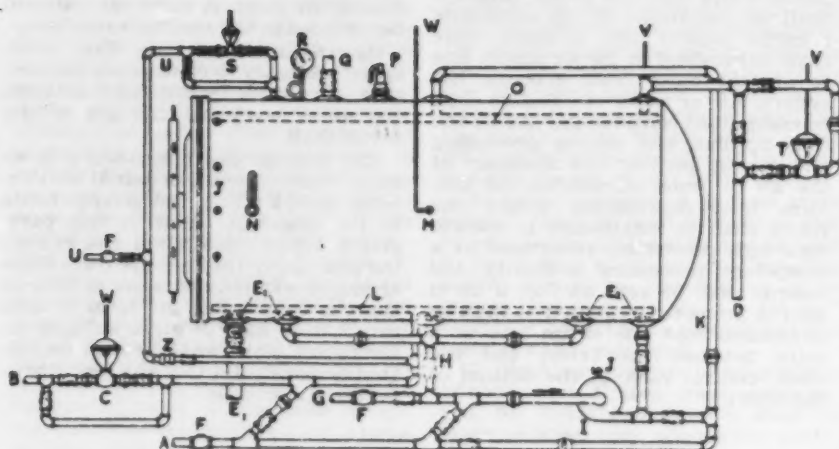
(12) *Retort headspace.* The headspace necessary to control the air pressure should be maintained between the water level and the top of the retort shell.

(13) *Vertical and horizontal still retorts.* Vertical and horizontal still retorts should follow the arrangements in the diagrams below in this paragraph. Other installation and operating procedures that deviate from these arrangements may be used, as long as there is evidence in the form of heat distribution data or other suitable information, which shall be kept on file, that demonstrates that the heat distribution is adequate.

Vertical Retorts



Horizontal Roterts



LEGEND FOR VERTICAL AND HORIZONTAL STILL
RETORTS

- A—Water line.
- B—Steam line.
- C—Temperature control.
- D—Overflow line.
- E—Drain line.
- F—Screens.
- G—Check valves.
- H—Line from hot water storage.
- I—Suction line and manifold.
- J—Circulating pump.
- K—Petcocks.
- L—Recirculating line.
- M—Steam distributor.
- N—Temperature-controller bulb.
- O—Thermometer.
- P—Water spreader.
- Q—Safety valve.
- R—Vent valve for steam processing.
- S—Pressure gage.
- T—Inlet air control.
- U—Pressure control.
- V—Air line.
- W—To pressure control instrument.
- X—To temperature control instrument.
- Y—Wing nuts.
- Z—Crate support.
- aa—Crate guides.
- bb—Constant flow orifice valve.
- cc—Constant flow orifice valve used during come-up.
- dd—Constant flow orifice valve used during cook.

(14) *Critical factors.* Critical factors specified in the scheduled process shall be measured and recorded on the processing record at intervals of sufficient frequency to ensure that the factors are within the limits specified in the scheduled process.

(i) When maximum fill-in or drained weight is specified in the scheduled process, it shall be measured and recorded at intervals of sufficient frequency to ensure that the weight of the product does not exceed the maximum for the given container size specified in the scheduled process.

(ii) Closing machine vacuum in vacuum-packed products shall be observed and recorded at intervals of sufficient frequency to ensure that the vacuum is as specified in the scheduled process.

(iii) Such measurements and recordings should be made at intervals not to exceed 15 minutes.

(iv) When the product style results in stratification or layering of the primary product in the containers, the positioning of containers in the retort

shall be according to the scheduled process.

(c) *Equipment and procedures for pressure processing in steam in continuous agitating retorts—*(1) *Indicating mercury-in-glass thermometer.* Each retort shall be equipped with at least one mercury-in-glass thermometer whose divisions are easily readable to 1° F and whose temperature range does not exceed 17° F per inch of graduated scale. Thermometers shall be tested for accuracy against a known accurate standard thermometer upon installation and at least once a year thereafter, or more frequently if necessary, to ensure their accuracy. Records of thermometer accuracy checks which specify date, standard used, method used, and person performing the test should be maintained. Each thermometer should have a tag, seal, or other means of identity that includes the date on which it was last tested for accuracy. A thermometer that has a divided mercury column or that cannot be adjusted to the standard shall be repaired or replaced before further use of the retort. Thermometers shall be installed where they can be accurately and easily read. Bulbs in indicating thermometers shall be installed either within the retort shell or in external wells attached to the retort. External wells or pipes shall be connected to the retort through at least a ¼-inch diameter opening, and equipped with a ⅛-inch or larger bleeder opening so located as to provide a full flow of steam past the length of the thermometer bulb. The bleeders for external wells shall emit steam continuously during the entire processing period. The mercury thermometer—not the recorder chart—shall be the reference instrument for indicating the processing temperature.

(2) *Temperature-recording device.* Each retort shall have an accurate temperature-recording device. Graduations on the temperature-recording devices shall not exceed 2° F within a range of 10° F of the processing temperature. Each chart shall have a working scale of not more than 55° F per inch within a range of 20° F of the processing temperature. The temperature chart shall be adjusted to agree

as nearly as possible with, but to be in no event higher than, the known accurate mercury-in-glass thermometer during the process time. A means of preventing unauthorized changes in adjustment shall be provided. A lock, or a notice from management posted at or near the recording device that provides a warning that only authorized persons are permitted to make adjustments, is a satisfactory means of preventing unauthorized changes. The recorder may be combined with the steam controller and may be a recording-controlling instrument. The temperature-recorder bulb shall be installed either within the retort shell or in a well attached to the shell. Each temperature-recorder bulb well shall have a $\frac{1}{8}$ -inch or larger bleeder opening emitting steam continuously during the processing period. Air-operated temperature controllers should have adequate filter systems to ensure a supply of clean, dry air.

(3) *Pressure gages.* Each retort should be equipped with a pressure gage that should be graduated in divisions of 2 pounds or less.

(4) *Steam controller.* Each retort shall be equipped with an automatic steam controller to maintain the retort temperature. This may be a recording-controlling instrument when combined with a recording thermometer. A steam controller activated by the steam pressure of the retort is acceptable if it is carefully maintained mechanically so that it operates satisfactorily.

(5) *Bleeders.* Bleeders, except those for thermometer wells, shall be one-eighth inch or larger and shall be wide open during the entire process, including the come-up-time. Bleeders shall be located within approximately 1 foot of the outermost location of containers at each end along the top of the retort; additional bleeders shall be located not more than 8 feet apart along the top of the retort. All bleeders shall be arranged so that the operator can observe that they are functioning properly. The condensate bleeder shall be checked with sufficient frequency to ensure adequate removal of condensate or shall be equipped with an automatic alarm system(s) that would serve as a continuous monitor of con-

densate-bleeder functioning. Visual checks should be done at intervals of not more than 15 minutes. A record of such checks should be kept to show that the bleeder is functioning properly.

(6) *Venting and condensate removal.* Vents shall be located in that portion of the retort opposite the steam inlet. Air shall be removed before processing is started. Heat distribution data or documentary proof from the manufacturer or from a competent processing authority, demonstrating that adequate venting is achieved, shall be kept on file. At the time steam is turned on, the drain should be opened for a time sufficient to remove steam condensate from the retort, and provision shall be made for continuing drainage of condensate during the retort operation. The condensate bleeder in the bottom of the shell serves as an indicator of continuous condensate removal.

(7) *Retort speed timing.* The rotational speed of the retort shall be specified in the scheduled process. The speed shall be adjusted and recorded when the retort is started, at any time a speed change is made, and at intervals of sufficient frequency to ensure that the retort speed is maintained as specified in the scheduled process. These adjustments and recordings should be made every 4 hours or less. Alternatively, a recording tachometer may be used to provide a continuous record of the speed. A means of preventing unauthorized speed changes on retorts shall be provided. A lock, or a notice from management posted at or near the speed adjustment device that provides a warning that only authorized persons are permitted to make adjustments, is a satisfactory means of preventing unauthorized changes.

(8) *Emergency stops.* If a retort jams or breaks down during processing operations, necessitating cooling the retort for repairs, the retort shall be operated in such a way that ensures that the product is commercially sterile, or the retort is to be cooled promptly and all containers either reprocessed, repacked and reprocessed, or discarded. When operated as a still retort, all containers shall be given a

ull still retort process before the retort is cooled. If, in such an emergency, a scheduled still process or another process established to ensure commercial sterility is to be used, it shall be made readily available to the retort operator.

(i) Any containers in the retort intake valve or in transfer valves between cooker shells of a continuous retort at the time of breakdown shall either be reprocessed, repacked and reprocessed, or discarded.

(ii) Both the time at which the reel stopped and the time the retort was used for a still retort process, if so used, shall be marked on the recording chart and entered on the other production records required in this chapter. If the alternative procedure of prompt cooling is followed, the subsequent handling methods used for the containers in the retort at the time of stopping and cooling shall be entered on the production records.

(9) *Temperature drop.* If the temperature of the continuous retort drops below the temperature specified in the scheduled process while containers are in the retort, the retort reel shall be stopped promptly. An automatic device should be used to stop the reel when the temperature drops below the specified process temperature. Before the reel is restarted, all containers in the retort shall be given a complete scheduled still retort process if the temperature drop was 10° F or more below the specified temperature, or alternatively, container entry to the retort shall be stopped and the reel restarted to empty the retort. The discarded containers shall be either reprocessed, repacked and reprocessed, or discarded. Both the time at which the reel stopped and the time the retort was used for a still retort process, if so used, shall be marked on the recording chart and entered on the other production records required in this chapter. If the alternative procedure of emptying the retort is followed, the subsequent handling methods used for the containers in the retort at the time of the temperature drop shall be entered on the production records. If the temperature drop is less than 10° F, a scheduled authorized emergency still process ap-

proved by a qualified person(s) having expert knowledge of thermal processing requirements may be used before restarting the retort reel. Alternatively, container entry to the retort shall be stopped and an authorized emergency agitating process may be used before container entry to the retort is restarted. When emergency procedures are used, no containers may enter the retort and the process and procedures used shall be noted on the production records.

(10) *Critical factors.* Critical factors specified in the scheduled process shall be measured and recorded on the processing record at intervals of sufficient frequency to ensure that the factors are within the limits specified in the scheduled process. The minimum headspace of containers, if specified in the scheduled process, shall be measured and recorded at intervals of sufficient frequency to ensure that the headspace is as specified in the scheduled process. The headspace of solder-tipped, lap seam (vent hole) cans may be measured by net weight determinations. The headspace of double seamed cans may also be measured by net weight determinations for homogeneous liquids, taking into account the specific can end profile and other factors which affect the headspace, if proof of the accuracy of such measurements is maintained and the procedure and resultant headspace is in accordance with the scheduled process. When the product consistency is specified in the scheduled process, the consistency of the product shall be determined by objective measurements on the product taken from the filler before processing and recorded at intervals of sufficient frequency to ensure that the consistency is as specified in the scheduled process. Minimum closing machine vacuum in vacuum-packed products, maximum fill-in or drained weight, minimum net weight, and percent solids shall be as specified in the scheduled process for all products when deviations from such specifications may affect the scheduled process. All measurements and recordings of critical factors should be made at intervals not to exceed 15 minutes.

(d) *Equipment and procedures for pressure processing in steam in discontinuous agitating retorts—(1) Indicating mercury-in-glass thermometer.* Each retort shall be equipped with at least one mercury-in-glass thermometer whose divisions are easily readable to 1° F and whose temperature range does not exceed 17° F per inch of graduated scale. Thermometers shall be tested for accuracy against a known accurate standard thermometer upon installation and at least once a year thereafter, or more frequently if necessary, to ensure their accuracy. Records of thermometer accuracy checks which specify date, standard used, method used, and person performing the test should be maintained. Each thermometer should have a tag, seal, or other means of identity that includes the date on which it was last tested for accuracy. A thermometer that has a divided mercury column or that cannot be adjusted to the standard shall be repaired or replaced before further use of the retort. Thermometers shall be installed where they can be accurately and easily read. Bulbs of indicating thermometers shall be installed either within the retort shell or in external wells attached to the retort. External wells or pipes shall be connected to the retort through at least a 3/4-inch-diameter opening, and equipped with a 1/4-inch or larger bleeder opening so located as to provide a full flow of steam past the length of the thermometer bulb. The bleeder for external wells shall emit steam continuously during the entire processing period. The mercury thermometer—not the recorder chart—shall be the reference instrument for indicating the processing temperature.

(2) *Temperature-recording device.* Each retort shall have an accurate temperature-recording device. Graduations on the temperature-recording devices shall not exceed 2° F within a range of 10° F of the processing temperature. Each chart shall have a working scale of not more than 55° F per inch within a range of 20° F of the processing temperature. The temperature chart shall be adjusted to agree as nearly as possible with, but to be in no event higher than, the known accu-

rate mercury-in-glass thermometer during the process time. A means of preventing unauthorized changes in adjustment shall be provided. A lock, or a notice from management posted at or near the recording device that provides a warning that only authorized persons are permitted to make adjustments, is a satisfactory means for preventing unauthorized changes. The recorder may be combined with the steam controller and may be a recording-controlling instrument. The temperature-recorder bulb shall be installed either within the retort shell or in a well attached to the shell. Each temperature-recorder bulb well shall have a 1/4-inch or larger bleeder opening emitting steam continuously during the processing period. Air-operated temperature controllers should have adequate filter systems to ensure a supply of clean, dry air.

(3) *Pressure gages.* Each retort should be equipped with a pressure gage, which should be graduated in divisions of 2 pounds or less.

(4) *Steam controller.* Each retort shall be equipped with an automatic steam controller to maintain the retort temperature. This may be a recording-controlling instrument when combined with a recording thermometer. A steam controller activated by the steam pressure of the retort is acceptable if it is mechanically maintained so that it operates satisfactorily.

(5) *Bleeders.* Bleeders, except those for thermometer wells, shall be one-eighth inch or larger and shall be wide open during the entire process, including the come-up-time. Bleeders shall be located within approximately 1 foot of the outermost location of containers at each end along the top of the retort; additional bleeders shall be located not more than 8 feet apart along the top. Bleeders may be installed at positions other than those specified above, as long as there is evidence in the form of heat distribution data that they accomplish adequate removal of air and circulation of heat within the retort. In retorts having top steam inlet and bottom venting, a bleeder shall be installed in the bottom of the retort to remove condensate. All bleeders shall be arranged in a way that en-

ables the operator to observe that they are functioning properly.

(6) *Venting and condensate removal.* The air in each retort shall be removed before processing is started. Heat distribution data or documentary proof from the manufacturer or from a competent processing authority, demonstrating that adequate venting is achieved, shall be kept on file. At the time steam is turned on, the drain should be opened for a time sufficient to remove steam condensate from the retort and provision should be made for continuing drainage of condensate during the retort operation.

(7) *Retort speed timing.* The rotational speed of the retort shall be specified in the scheduled process. The speed shall be adjusted, as necessary, to ensure that the speed is as specified in the scheduled process. The rotational speed as well as the process time shall be recorded for each retort load processed. Alternatively, a recording tachometer may be used to provide a continuous record of the speed. A means of preventing unauthorized speed changes on retorts shall be provided. A lock, or a notice from management posted at or near the speed-adjustment device that provides a warning that only authorized persons are permitted to make adjustments, is a satisfactory means of preventing unauthorized changes.

(8) *Critical factors.* Critical factors specified in the scheduled process shall be measured and recorded on the processing record at intervals of sufficient frequency to ensure that the factors are within the limits specified in the scheduled process. The minimum headspace of containers in each retort load to be processed, if specified in the scheduled process, shall be measured and recorded at intervals of sufficient frequency to ensure that the headspace is as specified in the scheduled process. The headspace of solder-lapped, lap seam (vent hole) cans may be measured by net weight determinations. When the product consistency is specified in the scheduled process, the consistency of the product shall be determined by objective measurements in the product taken from the filler before processing and recorded at intervals of sufficient frequency to

ensure that the consistency is as specified in the scheduled process. Minimum closing machine vacuum in vacuum-packed products, maximum fill-in or drained weight, minimum net weight, and percent solids shall be as specified in the scheduled process for all products for which deviations from such specifications may affect the scheduled process. All measurements and recordings of critical factors should be made at intervals not to exceed 15 minutes.

(c) *Equipment and procedures for pressure processing in water in discontinuous agitating retorts—(1) Indicating mercury-in-glass thermometer.* Each retort shall be equipped with at least one mercury-in-glass thermometer whose divisions are easily readable to 1° F and whose temperature range does not exceed 17° F per inch of graduated scale. Thermometers shall be tested for accuracy against a known accurate standard thermometer upon installation and at least once a year thereafter, or more frequently if necessary, to ensure their accuracy. Records of thermometer accuracy checks which specify date, standard use, method used, and person performing the test should be maintained. Each thermometer should have a tag, seal, or other means of identity that includes the date on which it was last tested for accuracy. A thermometer that has a divided mercury column or that cannot be adjusted to the standard shall be repaired or replaced before further use of the retort. Thermometers shall be installed where they can be accurately and easily read. Bulbs of indicating thermometers shall be installed either within the retort shell or in external wells attached to the retort. The mercury thermometer—not the recorder chart—shall be the reference instrument for indicating the processing temperature.

(2) *Temperature-recording device.* Each retort shall have an accurate temperature-recording device. Graduations on the temperature-recording devices shall not exceed 2° F within a range of 10° F of the processing temperature. Each chart shall have a working scale of not more than 55° F per inch within a range of 20° F of the

processing temperature. The temperature chart shall be adjusted to agree as nearly as possible with, but to be in no event higher than, the known accurate mercury-in-glass thermometer during the process time. A means of preventing unauthorized changes in adjustment shall be provided. A lock, or a notice from management posted at or near the recording device that provides a warning that only authorized persons are permitted to make adjustment, is a satisfactory means for preventing unauthorized changes. This recorder may be combined with the steam controller and may be a recording-controlling instrument. The temperature-recorder bulb shall be installed either within the retort shell or in a well attached to the shell. Air-operated temperature controllers should have adequate filter systems to ensure a supply of clean dry air.

(3) *Pressure gages.* Each retort should be equipped with a pressure gage which should be graduated in divisions of 2 pounds or less.

(4) *Steam controller.* Each retort shall be equipped with an automatic steam controller to maintain the retort temperature. This may be a recording-controlling instrument when combined with a recording thermometer.

(5) *Retort speed timing.* The rotational speed of the retort shall be specified in the scheduled process. The speed shall be adjusted, as necessary, to ensure that the speed is as specified in the scheduled process. The rotational speed as well as the process time shall be recorded for each retort load processed. Alternatively, a recording tachometer may be used to provide a continuous record of the speed. A means of preventing unauthorized speed changes shall be provided. A lock, or a notice from management posted at or near the speed adjustment device that provides a warning that only authorized persons are permitted to make adjustment, is a satisfactory means of preventing unauthorized changes.

(6) *Air supply and controls.* Means shall be provided for introducing compressed air at the proper pressure and rate, which shall be controlled by an automatic pressure control unit. A

check value shall be provided in the air supply line to prevent water from entering the system.

(7) *Critical factors.* Critical factors specified in the scheduled process shall be measured and recorded on the processing record at intervals of sufficient frequency to ensure that the factors are within the limits specified in the scheduled process. The minimum headspace of containers, if specified in the scheduled process, shall be measured and recorded at intervals of sufficient frequency to ensure that the headspace is as specified in the scheduled process. The headspace of solder-tipped, lap seam (vent hole) cans may be measured by net weight determinations. When the product consistency is specified in the scheduled process, the consistency of the product shall be determined by objective measurements on the product taken from the filler before processing and recorded at intervals of sufficient frequency to ensure that the consistency is as specified in the scheduled process. Minimum closing machine vacuum in vacuum-packed products, maximum fill-in or drained weight, minimum net weight, and percent solids shall be as specified in the scheduled process for all products when deviations from such specifications may affect the scheduled process. All measurements and recordings of critical factors should be made at intervals not to exceed 15 minutes.

(f) *Equipment and procedures for pressure processing in steam in hydrostatic retorts—(1) Indicating mercury-in-glass thermometer.* Each retort shall be equipped with at least one mercury-in-glass thermometer whose divisions are easily readable to 1° F and whose temperature range does not exceed 17° F per inch of graduated scale. Thermometers shall be tested for accuracy against a known accurate standard thermometer upon installation and at least once a year thereafter, or more frequently if necessary, to ensure their accuracy. Records of thermometer accuracy checks which specify date, standard used, method used, and person performing the test should be maintained. Each thermometer should have a tag, seal, or other means of identity that includes the

date on which it was last tested for accuracy. A thermometer that has a divided mercury column or that cannot be adjusted to the standard shall be repaired or replaced before further use of the retort. Thermometers shall be installed where they can be accurately and easily read. The thermometer shall be located in the steam dome near the steam-water interface. When the scheduled process specifies maintenance of particular temperatures in the hydrostatic water legs, a mercury-in-glass thermometer shall be located in each hydrostatic water leg in a position near the bottom automatic recorder. The mercury thermometer—not the recorder chart—shall be the reference instrument for indicating the processing temperature.

(2) *Temperature-recording device.* Each retort shall have an accurate temperature-recording device. Graduations on the temperature-recording devices shall not exceed 2° F within a range of 10° F of the processing temperature. Each chart shall have a working scale of not more than 55° F per inch within a range of 20° F of the processing temperature. The temperature chart shall be adjusted to agree as nearly as possible with, but to be in no event higher than, the known accurate mercury-in-glass thermometer during the process time. A means of preventing unauthorized changes in adjustment shall be provided. A lock, or a notice from management posted at or near the recording device that provides a warning that only authorized persons are permitted to make adjustments, is a satisfactory means for preventing unauthorized changes. The recorder may be combined with the steam controller and may be a recording-controlling instrument. The temperature-recorder bulb shall be installed either within the steam dome or in a well attached to the dome. Each temperature-recorder bulb well shall have a 1/4-inch or larger bleeder opening which emits steam continuously during the processing period. Additional temperature-recorder bulbs shall be installed in the hydrostatic water legs if the scheduled process specifies maintenance of particular temperatures in the hydrostatic water

trollers should have adequate filter systems to ensure a supply of clean dry air.

(3) *Pressure gages.* Each retort should be equipped with a pressure gage which should be graduated in divisions of 2 pounds or less.

(4) *Recording of temperatures.* Temperatures indicated by the mercury-in-glass thermometer or thermometers shall be entered on a suitable form during processing operations. Temperatures shall be recorded by an accurate automatic recorder or recorders at the following points:

(i) In the steam chamber between the steam-water interface and the lowest container position.

(ii) Near the top and the bottom of each hydrostatic water leg if the scheduled process specifies maintenance of particular temperatures in the legs.

(5) *Steam controller.* Each retort shall be equipped with an automatic steam controller to maintain the retort temperature. This may be a recording-controlling instrument when combined with a recording thermometer. A steam controller activated by the steam pressure of the retort is acceptable if it is carefully mechanically maintained so that it operates satisfactorily.

(6) *Venting.* Before the start of processing operations, the retort steam chamber or chambers shall be vented to ensure removal of air.

(7) *Bleeders.* Bleeder openings 1/4-inch or larger shall be located at the top of the steam chamber or chambers opposite the point of steam entry. Bleeders shall be wide open and shall emit steam continuously during the entire process, including the come-up time. All bleeders shall be arranged in such a way that the operator can observe that they are functioning properly.

(8) *Retort speed.* The speed of the container-conveyor chain shall be specified in the scheduled process and shall be determined and recorded at the start of processing and at intervals of sufficient frequency to ensure that the retort speed is maintained as specified. The speed should be determined and recorded every 4 hours. An automatic device should be used to stop

the chain when the temperature drops below that specified in the scheduled process. A means of preventing unauthorized speed changes shall be provided. A lock, or a notice from management posted at or near the speed-adjusting device that provides a warning that only authorized persons are permitted to make adjustments, is a satisfactory means of preventing unauthorized changes.

(9) *Critical factors.* Critical factors specified in the scheduled process shall be measured and recorded on the processing record at intervals of sufficient frequency to ensure that the factors are within the limits specified in the scheduled process.

(i) When maximum fill-in or drained weight is specified in the scheduled process, it shall be measured and recorded at intervals of sufficient frequency to ensure that the weight of the product does not exceed the maximum for the given container size specified in the scheduled process.

(ii) Closing machine vacuum in vacuum-packed products shall be observed and recorded at intervals of sufficient frequency to ensure that the vacuum is as specified in the scheduled process.

(iii) Such measurements and recordings should be made at intervals not to exceed 15 minutes.

(g) *Aseptic processing and packaging systems—(1) Product sterilizer—(i) Equipment—(a) Temperature-indicating device.* Each product sterilizer shall be equipped with at least one mercury-in-glass thermometer or an equivalent temperature-indicating device, such as a thermocouple-recorder. Mercury-in-glass thermometers shall have divisions that are easily readable to 1° F and whose temperature range does not exceed 17° F per inch of graduated scale. Thermometers and temperature-indicating devices shall be tested for accuracy against a known accurate standard thermometer upon installation and at least once a year thereafter, or more frequently if necessary, to ensure their accuracy. Records of accuracy checks which specify date, standard used, method used, and person performing the test should be maintained. Each thermometer and temperature-indicating

device should have a tag, seal, or other means of identity that includes the date on which it was last tested for accuracy. A thermometer that has a divided mercury column or that cannot be adjusted to essential agreement with the standard shall be repaired or replaced. Thermometers and temperature-indicating devices shall be installed where they can be accurately and easily read. The temperature-indicating device shall be the reference instrument for indicating the processing temperature.

(b) *Temperature-recording device.* There shall be an accurate temperature recording device on each product sterilizer. The device shall be installed in the product at the holding-tube outlet between the holding tube and the inlet to the cooler. Temperature-recording devices shall have graduations that do not exceed 2° F within a range of 10° F of the processing temperature. Each chart shall have a working scale of not more than 55° F per inch within a range of 20° F of the desired product-sterilization temperature. The temperature chart shall be adjusted to agree as nearly as possible with, but to be in no event higher than, a known accurate mercury-in-glass thermometer. A means of preventing unauthorized changes in adjustment shall be provided. A lock, or a notice from management posted at or near the recording device that provides a warning that only authorized persons are permitted to make adjustments, is a satisfactory means for preventing unauthorized changes.

(c) *Temperature recorder-controller.* An accurate temperature recorder-controller shall be located in the product sterilizer at the final heater outlet. It shall be capable of ensuring that the desired product sterilization temperature is maintained. The chart graduations shall not exceed 2° F within a range of 10° F of the desired product sterilization temperature. Air-operated temperature controllers should have adequate filter systems to ensure a supply of clean, dry air.

(d) *Product-to-product regenerators.* When a product-to-product regenerator is used to heat the cold unsterilized product entering the sterilizer by means of a heat exchange system, it

shall be designed, operated, and controlled so that the pressure of the sterilized product in the regenerator is greater than the pressure of any unsterilized product in the regenerator to ensure that any leakage in the regenerator is from the sterilized product into the unsterilized product.

(e) *Differential pressure recorder-controller.* When a product-to-product regenerator is used, there shall be an accurate differential pressure recorder-controller installed on the regenerator. The scale divisions shall not exceed 2 pounds per square inch on the working scale of not more than 20 pounds per square inch per inch. The controller shall be tested for accuracy against a known accurate standard pressure indicator upon installation and at least once every 3 months of operation thereafter, or more frequently if necessary, to ensure its accuracy. One pressure sensor shall be installed at the sterilized product regenerator outlet and the other pressure sensor shall be installed at the unsterilized product regenerator inlet.

(f) *Metering pump.* A metering pump shall be located upstream from the holding tube and shall be operated to maintain the required rate of product flow. A means of preventing unauthorized speed changes shall be provided. A lock, or a notice from management posted at or near the speed-adjusting device that provides a warning that only authorized persons are permitted to make adjustments, is a satisfactory means of preventing unauthorized changes.

(g) *Product holding tube.* The product-sterilizing holding tube shall be designed to give continuous holding of every particle of food for at least the minimum holding time specified in the scheduled process. The holding tube shall be designed so that no portion of the tube between the product inlet and the product outlet can be heated, and it must be sloped upward at least 25 inch per foot.

(h) *Flow-diversion systems.* If a processor elects to install a flow-diversion system, it should be installed in the product piping located between the product cooler and the product filler or aseptic surge tank and should be designed to divert flow away from the

filler or aseptic surge tank automatically. Controls and/or warning systems should be designed and installed with necessary sensors and actuators to operate whenever the sterilizing temperature in the holding tube or pressure differential in the product regenerator drops below specified limits. Flow-diversion systems should be designed and operated in accordance with recommendations of an aseptic processing and packaging authority.

(i) *Equipment downstream from the holding tube.* Product coolers, aseptic surge tanks, or any other equipment downstream from the holding tube, with rotating or reciprocating shafts, valve stems, instrument connections, or other such points, are subject to potential entry of microorganisms into the product. Such locations in the system should be equipped with steam seals or other effective barriers at the potential access points. Appropriate means should be provided to permit the operator to monitor the performance of the seals or barriers during operation.

(ii) *Operation—(a) Startup.* Before the start of aseptic processing operations the product sterilizer and all product-contact surfaces downstream shall be brought to a condition of commercial sterility.

(b) *Temperature drop in product-sterilizing holding tube.* When product temperature in the holding tube drops below the temperature specified in the scheduled process, product flow should be diverted away from the filler or aseptic surge tank by means of a flow-diversion system. If for any reason product subjected to a temperature drop below the scheduled process is filled into containers, the product shall be segregated from product that received the scheduled process. The processing deviation shall be handled in accordance with § 507.89. The product holding tube and any further system portions affected shall be returned to a condition of commercial sterility before product flow is resumed to the filler or to the aseptic surge tank.

(c) *Loss of proper pressures in the regenerator.* When a regenerator is used, the product may lose sterility whenever the pressure of sterilized product

in the regenerator is less than 1 pound per square inch greater than the pressure of unsterilized product in the regenerator. In this case, product flow should be diverted away from the filler or aseptic surge tank by means of the flow-diversion system. If for any reason the product is filled into containers, the product shall be segregated from product that received the scheduled process and shall be reprocessed or destroyed. Product flow to the filler or to the aseptic surge tank shall not be resumed until the cause of the improper pressure relationships in the regenerator has been corrected and the affected system(s) has been returned to a condition of commercial sterility.

(d) *Loss of sterile air pressure or other protection level in the aseptic surge tank.* When an aseptic surge tank is used, conditions of commercial sterility may be lost when the sterile air overpressure or other means of protection drops below the scheduled process value. Product flow to and/or from the aseptic surge tank shall not be resumed until the potentially contaminated product in the tank is removed, and the aseptic surge tank has been returned to a condition of commercial sterility.

(e) *Records.* Readings at the following points shall be observed and recorded at the start of aseptic packaging operations and at intervals of sufficient frequency to ensure that these values are as specified in the scheduled process: Temperature-indicating device in holding tube outlet; temperature recorder in holding tube outlet; temperature recorder-controller at final heater outlet; differential pressure recorder-controller, if a product-to-product regenerator is used; product flow rate as established by the metering pump or as determined by filling and closing rates and, if an aseptic surge tank is used, sterile air pressure or other protection means; and proper performance of seam seals or other similar devices. The measurements and recordings should be made at intervals not to exceed 1 hour.

(2) *Container sterilizing, filling, and closing operation—(i) Equipment—(a) Recording device.* The container and closure sterilization system and prod-

uct filling and closing system shall be instrumented to demonstrate that the required sterilization is being accomplished continuously. Automatic recording devices shall be used to record, when applicable, the sterilization media flow rates, temperature, concentration, or other factors. When a batch system is used for container sterilization, the sterilization conditions shall be recorded.

(b) *Timing method(s).* A method(s) shall be used either to give the retention time of containers, and closures if applicable, in the sterilizing environment specified in the scheduled process, or to control the sterilization cycle at the rate specified in the scheduled process. A means of preventing unauthorized speed changes must be provided. A lock, or a notice from management posted at or near the speed adjusting device that provides a warning that only authorized persons are permitted to make adjustments, is a satisfactory means of preventing unauthorized changes.

(ii) *Operation—(a) Startup.* Before the start of packaging operations, both the container and closure sterilizing system and the product filling and closing system shall be brought to a condition of commercial sterility.

(b) *Loss of sterility.* A system shall be provided to stop packaging operations, or alternatively to ensure segregation of any product packaged when the packaging conditions fall below scheduled processes. Compliance with this requirement may be accomplished by diverting product away from the filler, by preventing containers from entering the filler, or by other suitable means. In the event product is packaged under conditions below those specified in the scheduled process, all such product shall be segregated and handled in accordance with § 507.89. In the event of loss of sterility, the system(s) shall be returned to a condition of commercial sterility before resuming packaging operations.

(c) *Records.* Observations and measurements of operating conditions shall be made and recorded at intervals of sufficient frequency to ensure that commercial sterility of the food product is being achieved; such measure-

ments shall include the sterilization media flow rates, temperatures, the container and closure rates (if applicable) through the sterilizing system, and the sterilization conditions if a batch system is used for container sterilization. The measurements and recordings should be made at intervals not to exceed 1 hour.

(3) *Incubation*. Incubation tests should be conducted on a representative sample of containers of product from each code; records of the test results should be maintained.

(4) *Critical factors*. Critical factors specified in the scheduled process shall be measured and recorded on the processing record at intervals of sufficient frequency to ensure that the factors are within the limits specified in the scheduled process. Such measurements and recordings should be done at intervals not to exceed 15 minutes.

(h) *Equipment and procedures for flame sterilizers*. The container conveyor speed shall be specified in the scheduled process. The container conveyor speed shall be measured and recorded at the start of operations and at intervals of sufficient frequency to ensure that the conveyor speed is as specified in the scheduled process. Such measurements and recordings should be done at 1-hour intervals. Alternatively, a recording tachometer may be used to provide a continuous record of the speed. A means of preventing changes in flame intensity and unauthorized speed changes on the conveyor shall be provided. A lock, or a notice from management posted at or near the speed adjusting device that provides a warning that only authorized persons are permitted to make adjustments, is a satisfactory means of preventing unauthorized changes. The surface temperature of at least one container from each conveyor channel shall be measured and recorded at the entry and at the end of the holding period at intervals of sufficient frequency to ensure that the temperatures specified in the scheduled process are maintained. Such measurements and recordings should be done at intervals not to exceed 15 minutes.

(1) *Process interruption*. In the event of process interruption wherein

the temperature of the product may have dropped, an authorized, scheduled emergency plan approved by a qualified person having expert knowledge of the process requirements may be used.

(2) *Critical factors*. Critical factors specified in the scheduled process shall be measured and recorded on the processing record at intervals of sufficient frequency to ensure that the factors are within the limits specified in the scheduled process.

(i) *Equipment and procedures for thermal processing of foods wherein critical factors such as water activity are used in conjunction with thermal processing*. The methods and controls used for the manufacture, processing, and packing of such foods shall be as established in the scheduled process and shall be operated or administered in a manner adequate to ensure that the product is safe. The time and temperature of processing and other critical factors specified in the scheduled process shall be measured with instruments having the accuracy and dependability adequate to ensure that the requirements of the scheduled process are met. All measurements shall be made and recorded at intervals of sufficient frequency to ensure that the critical factors are within the limits specified in the scheduled process.

(j) *Other systems*. All systems, whether or not specifically mentioned in this part, for the thermal processing of low-acid foods in hermetically sealed containers shall conform to the applicable requirements of this part and the methods and controls used for the manufacture, processing, and packing of these foods shall be as established in the scheduled process. These systems shall be operated or administered in a manner adequate to ensure that commercial sterility is achieved. Critical factors specified in the scheduled process shall be measured and recorded at intervals of sufficient frequency to ensure that the critical factors are within the limits specified in the scheduled process.

**Subpart D—Control of Components,
Food Product Containers, Clo-
sures, and In-Process Materials**

§ 507.60 Containers.

(a) *Closures.* Regular observations shall be maintained during production runs for gross closure defects. Any such defects shall be recorded and corrective action taken and recorded. At intervals of sufficient frequency to ensure proper closure, the operator, closure supervisor, or other qualified container closure inspection person shall visually examine either the top seam of a can randomly selected from each seaming head or the closure of any other type of container being used and shall record the observations made. For double-seam cans, each can should be examined for cutover or sharpness, skidding or deadheading, false seam, droop at the crossover or lap, and condition of inside of countersink wall for evidence of broken chuck. Such measurements and recordings should be made at intervals not to exceed 30 minutes. Additional visual closure inspections shall be made immediately following a jam in a closing machine, after closing machine adjustment, or after startup of a machine following a prolonged shutdown. All pertinent observations shall be recorded. When irregularities are found, the corrective action shall be recorded.

(1) Teardown examinations for double-seam cans shall be performed by a qualified individual and the results therefrom shall be recorded at intervals of sufficient frequency on enough containers from each seaming station to ensure maintenance of seam integrity. Such examinations and recordings should be made at intervals not to exceed 4 hours. The results of the teardown examinations shall be recorded and the corrective action taken, if any, shall be noted.

(i) Required and optional can seam measurements:

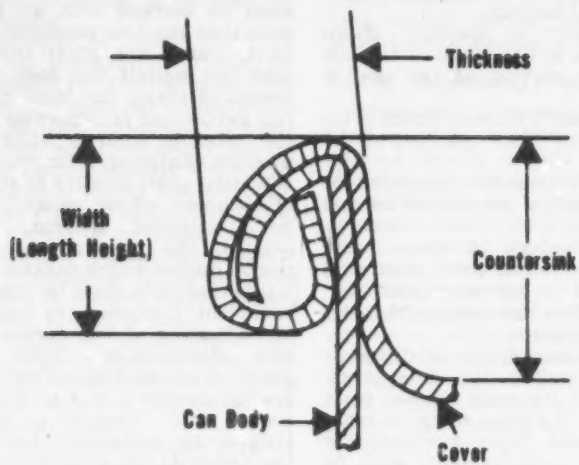
(a) **Micrometer measurement system:**

Required	Optional
Cover hook	Overlap (by calculation).
Body hook	Countersink.
Width (length, height)	
Tightness (observation for wrinkle)	
Thickness	

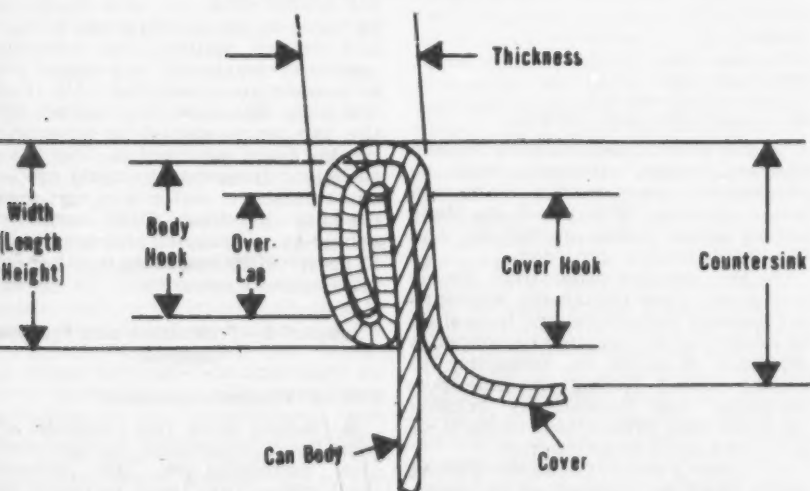
(b) **Seam scope or projector:**

Required	Optional
Body hook	Width (length, height).
Overlap	Cover hook.
Tightness (observation for wrinkle)	
Countersink	
Thickness by micrometer	

FIRST OPERATION ROLL SEAM



SECOND OPERATION ROLL SEAM



(c) Can double seam terminology:

(1) "Crossover": The portion of a double seam at the lap.

(2) "Cutover": A fracture, sharp bend, or break in the metal at the top of the inside portion of the double seam.

(3) "Deadhead": A seam which is incomplete due to chuck spinning in the countersink.

(4) "Droop": Smooth projection of double seam below bottom of normal seam.

(5) "False seam": A small seam breakdown where the cover hook and the body hook are not overlapped.

(6) "Lap": Two thicknesses of material bonded together.

(i) Two measurements at different locations, excluding the side seam, shall be made for each double seam characteristic if a seam scope or seam projector is used. When a micrometer is used, three measurements shall be made at points approximately 120° apart, excluding the side seam.

(ii) Overlap length can be calculated by the following formula:

$$\text{The theoretical overlap length} = CH + BH + T - W,$$

where

CH = cover hook

BH = body hook

T = cover thickness, and

W = seam width (height, length)

(2) For glass containers with vacuum closures, capper efficiency must be checked by a measurement of the cold water vacuum. This shall be done before actual filling operations, and the results shall be recorded.

(3) For closures other than double seams and glass containers, appropriate detailed inspections and tests shall be conducted by qualified personnel at intervals of sufficient frequency to ensure proper closing machine performance and consistently reliable hermetic seal production. Records of such tests shall be maintained.

(b) *Cooling water.* Container cooling water shall be chlorinated or otherwise sanitized as necessary for cooling canals and for recirculated water supplies. There should be a measurable residual of the sanitizer employed at the water discharge point of the container cooler.

(c) *Coding.* Each hermetically sealed container of low-acid processed food shall be marked with an identifying code that shall be permanently visible to the naked eye. When the container does not permit the code to be embossed or inked, the label may be legibly perforated or otherwise marked, if the label is securely affixed to the product container. The required identification shall identify in code the establishment where packed, the product contained therein, the year packed, the day packed, and the period during which packed. The packing period code shall be changed with sufficient frequency to enable ready identification of lots during their sale and distribution. Codes may be changed on the basis of one of the following: intervals of 4 to 5 hours; personnel shift changes; or batches, as long as the containers that constitute the batch do not extend over a period of more than one personnel shift.

(d) *Postprocess handling.* When cans are handled on belt conveyors, the conveyors should be so constructed as to minimize contact by the belt with the double seam, i.e., cans should not be rolled on the double seam. All worn and frayed belting, can retarders, cushions, etc. should be replaced with new nonporous material. All tracks and belts that come into contact with the can seams should be thoroughly scrubbed and sanitized at intervals of sufficient frequency to avoid product contamination. Automatic equipment used in handling filled containers should be so designed and operated as to preserve the can seam or other container closure integrity.

Subpart E—Production and Process Controls

§ 507.81 Product preparation.

(a) Before using raw materials and ingredients susceptible to microbiological contamination, the processor shall ensure that those materials and ingredients are suitable for use in processing low-acid food. Compliance with this requirement may be accomplished by receiving the raw materials and ingredients under a supplier's guarantee that they are suitable for

use, by examining them for their microbiological condition, or by other acceptable means.

(b) Blanching by heat, when required in the preparation of food for canning, should be effected by heating the food to the required temperature, holding it at this temperature for the required time, and then either rapidly cooling the food or passing it to subsequent processing without delay. Thermophilic growth and contamination in blanchers should be minimized by the use of adequate operating temperatures and by cleaning. If the blanched food product is washed before filling, potable water should be used.

(c) The filling of containers, either mechanically or by hand, shall be controlled so as to ensure that the filling requirements specified in the scheduled process are met.

(d) The exhausting of containers for the removal of air shall be controlled so as to meet the conditions for which the process was designed. Compliance with the requirement may be accomplished by heat exhausting, mechanical exhausting, hot brining, or steam injection.

(e) When the maintenance of pH above 4.6 of a normally low-acid food is a basis for a scheduled process, there shall be careful supervision to ensure that the equilibrium pH of the finished product meets that of the scheduled process. The methodology prescribed in § 114.90 of this chapter could be used.

(f) When the scheduled process sets forth critical factors to prevent the growth of microorganisms not destroyed by the thermal process, the factors shall be carefully controlled to ensure that the limits established in the scheduled process are not exceeded.

When normally low-acid foods require sufficient solute to permit safe processing at low temperatures, such as in boiling water, there shall be careful supervision to ensure that the equilibrium water activity (a_w) of the finished product meets that of the scheduled process. The scheduled thermal processes for foods having an a_w greater than 0.85 and less than the a_w that would allow the growth of spores of microorganisms of public health significance shall be sufficient

to render the food free of microorganisms capable of reproducing in the food under normal nonrefrigerated conditions of storage and distribution.

§ 507.83 Establishing scheduled processes.

Scheduled processes for low-acid foods shall be established by qualified persons having expert knowledge of thermal processing requirements for low-acid foods in hermetically sealed containers and having adequate facilities for making such determinations. The type, range, and combination of variations encountered in commercial production shall be adequately provided for in establishing the scheduled process. Critical factors, e.g., minimum headspace, consistency, maximum fill-in or drained weight, a_w , etc., that may affect the scheduled process, shall be specified in the scheduled process. Acceptable scientific methods of establishing heat sterilization processes shall include, when necessary, but shall not be limited to, microbial thermal death time data, process calculations based on product heat penetration data, and inoculated packs. Calculation shall be performed according to procedures recognized by competent processing authorities. If incubation tests are necessary for process confirmation, they shall include containers from test trials and from actual commercial production runs during the period of instituting the process. The incubation tests for confirmation of the scheduled processes should include the containers from the test trials and a number of containers from each of four or more actual commercial production runs. The number of containers from actual commercial production runs should be determined on the basis of recognized scientific methods to be of a size sufficient to ensure the adequacy of the process. Complete records covering all aspects of the establishment of the process and associated incubation tests shall be prepared and shall be permanently retained by the person or organization making the determination.

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§ 507.87 Operations in the thermal processing room.

(a) Operating processes and retort venting procedures to be used for each product and container size being packed shall either be posted in a conspicuous place near the processing equipment or be made readily available to the retort or processing system operator and any duly authorized employee of the Food and Drug Administration. Scheduled processes must be made readily available to the supervisor and any duly authorized employee of the Food and Drug Administration.

(b) A system for product traffic control in the retort room shall be established to prevent unretorted product from bypassing the retort process. Each retort basket, truck, car, or crate used to hold containers in a retort, or one or more containers therein, shall, if it contains any retorted food product, be plainly and conspicuously marked with a heat-sensitive indicator, or by other effective means that will indicate visually, to thermal processing personnel, those units that have been retorted. A visual check shall be performed to determine whether or not the appropriate change has occurred in the heat-sensitive indicator as a result of retorting for all retort baskets, trucks, cars, or crates, to ensure that each unit of product has been retorted. A written record of these checks should be made.

(c) The initial temperature of the contents of the containers to be processed shall be determined and recorded with sufficient frequency to ensure that the temperature of the product is no lower than the minimum initial temperature specified in the scheduled process. For those operations that use water during the filling of the retort or during processing, provision shall be made to ensure that the water will not, before the start of each thermal process, lower the initial temperature of the product below that specified in the scheduled process.

(d) Timing devices used in recording thermal process time information shall be accurate to the extent needed to ensure that the processing time and venting time specified in the scheduled process are achieved. Pocket or wrist watches are not considered satis-

factory for timing purposes. Digital clocks may be used if the operating process and the venting schedule have a 1-minute or greater safety factor over the scheduled process.

(e) Clock times on recording-temperature charts should reasonably correspond to the time of day on the written processing records to provide correlation of these records.

(f) The steam supply to the thermal processing system shall be adequate to the extent needed to ensure that sufficient steam pressure is maintained during thermal processing, regardless of other demands of steam by the plant.

(g) If mufflers are used on bleeders or vent systems, evidence that the bleeders or vents are operated in a manner that does not significantly impede the removal of air shall be kept on file. This evidence may be in the form of heat distribution data or other satisfactory evidence such as a letter from the manufacturer, the designer, or a competent processing authority.

§ 507.89 Deviations in processing, venting, or control of critical factors.

Whenever any process is less than the scheduled process or when critical factors are out of control for any low-acid food or container system as disclosed from records by processor check or otherwise, the commercial processor of that low-acid food shall either fully reprocess that portion of the production involved, keeping full records of the reprocessing conditions or, alternatively, shall set aside that portion of the product involved for further evaluation as to any potential public health significance. Such evaluation shall be made by a competent processing authority and shall be in accordance with procedures recognized by competent processing authorities as being adequate to detect any potential hazard to public health. Unless this evaluation demonstrates that the product had been given a thermal process that rendered it free of microorganisms of potential public health significance, the product set aside shall be either fully reprocessed to render it commercially sterile or de-

employed. A record shall be made of the evaluation procedures used and the results. Either upon completion of full processing and the attainment of commercial sterility or after the determination that no significant potential public health hazard exists, that portion of the product involved may be shipped in normal distribution. Otherwise, the portion of the product involved shall be destroyed. All procedures involving a failure to satisfy the minimum requirements of the scheduled process, including emergencies arising from a jam or breakdown of a continuous agitating retort necessitating cooling the retort for repairs, shall be recorded and made the subject of a separate file (or a log identifying the appropriate data) defining those deviations and the actions taken.

Subpart F—Records and Reports

§ 507.100 Processing and production records.

(a) Processing and production information shall be entered at the time it is observed by the retort or processing system operator, or other designated person, on forms that include the product, the code number, the date, the retort or processing system number, the size of container, the approximate number of containers per holding interval, the initial temperature, the actual processing time, the mercury-in-glass and recording thermometer readings, and other appropriate processing data. Closing machine vacuum in vacuum-packed products, maximum fill-in or drained weight, or other critical factors specified in the scheduled process shall also be recorded.

In addition, the following records shall be maintained:

(1) *Still retorts.* Time steam on; time temperature up to processing temperature; time steam off; venting time and temperature to which vented.

(2) *Agitating retorts.* Functioning of condensate bleeder; retort speed; and, when specified in the scheduled process, headspace, consistency, maximum drained weight, minimum net weight, and percent solids.

(3) *Hydrostatic retorts.* The temperature in the steam chamber between

the steam-water interface and the lowest container position; speed of the container conveyor chain; and, when the scheduled process specifies maintenance of particular temperatures in the hydrostatic water legs, the temperatures near the top and the bottom of each hydrostatic water leg.

(4) *Aseptic processing and packaging systems.* Product temperature in the holding tube outlet as indicated by the temperature-indicating device and the temperature recorder; product temperature in the final heater outlet as indicated by the temperature recorder-controller; differential pressure as indicated by the differential pressure recorder-controller, if a product-to-product regenerator is used; product flow rate, as determined by the metering pump or by filling and closing rates; sterilization media flow rate or temperature or both; retention time of containers, and closures when applicable, in the sterilizing environment; and, when a batch system is used for container and/or closure sterilization, sterilization cycle times and temperatures.

(5) *Flame sterilizers.* Container conveyor speed; surface temperature at the beginning and at the end of the holding period; nature of container.

(6) *Food preservation methods wherein critical factors such as water activity are used in conjunction with thermal processing.* Product formulation and scheduled processes used, including the thermal process, its associated critical factors, as well as other critical factors, and results of a, determinations.

(7) *Other systems.* Critical factors specified in the formulation of the product or in the scheduled process.

(b) Recording thermometer charts shall be identified by date, retort number, and other data as necessary, so they can be correlated with the written record of lots processed. Each entry on the processing and production records shall be made by the retort or processing system operator, or other designated person, at the time the specific retort or processing system condition or operation occurs, and this retort or processing system operator or other designated person shall sign or initial each record form.

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Not later than 1 working day after the actual process, and before shipment or release for distribution, a representative of plant management who is qualified by suitable training or experience shall review all processing and production records for completeness and to ensure that the product received the scheduled process. The records, including the recording thermometer chart(s), shall be signed or initialed and dated by the reviewer.

(c) Written records of all container closure examinations shall specify the product code, the date and time of container closure inspections, the measurements obtained, and all corrective actions taken. Records shall be signed or initialed by the container closure inspector and reviewed by management with sufficient frequency to ensure that the containers are hermetically sealed.

(d) Records shall be maintained to identify the initial distribution of the finished product to facilitate, when necessary, the segregation of specific food lots that may have become contaminated or otherwise rendered unfit for their intended use.

(e) Copies of all records provided for in this part, except those required under § 507.83 establishing scheduled processes, shall be retained at the processing plant for a period of not less than 1 year from the date of manufacture, and at the processing plant or other reasonably accessible location for an additional 2 years. If, during the first year of the 3-year record-retention period, the processing plant is closed for a prolonged period between seasonal packs, the records may be transferred to some other reasonably accessible location at the end of the seasonal pack.

PART 508—EMERGENCY PERMIT CONTROL

Subpart A—General Provisions

- Sec.
- 508.3 Definitions.
- 508.5 Determination of the need for a permit.
- 508.6 Revocation of determination of need for permit.
- 508.7 Issuance or denial of permit.

Sec.

- 508.10 Suspension and reinstatement of permit.
- 508.12 Manufacturing, processing, or packing without a permit or in violation of a permit.
- 508.19 Establishment of requirements for exemption from section 404 of the act.

Subpart B—Requirements and Conditions for Exemption From or Compliance With an Emergency Permit

- 508.35 Thermal processing of low-acid animal foods packaged in hermetically sealed containers.

AUTHORITY: Secs. 402, 404, 701, 52 Stat. 1046-1047 as amended, 1048, 1055-1056 as amended by 70 Stat. 919 and 72 Stat. 948; 21 U.S.C. 342, 344, 371.

SOURCE: 41 FR 38637, Sept. 10, 1976, unless otherwise noted.

Subpart A—General Provisions

§ 508.3 Definitions.

(a) The definitions contained in section 201 of the Federal Food, Drug, and Cosmetic Act are applicable to such terms when used in this part.

(b) "Commissioner" means the Commissioner of Food and Drugs.

(c) "Act" means the Federal Food, Drug, and Cosmetic Act, as amended.

(d) "Permit" means an emergency permit issued by the Commissioner pursuant to section 404 of the act for such temporary period of time as may be necessary to protect the public health.

(e) "Manufacture, processing, or packing of food in any locality" means activities conducted in a single plant or establishment, a series of plants under a single management, or all plants in an industry or region, by a manufacturer, processor, or packer.

§ 508.5 Determination of the need for a permit.

(a) Whenever the Commissioner determines after investigation that a manufacturer, processor, or packer of a food for which a regulation has been promulgated in Subpart B of this part does not meet the mandatory conditions and requirements established in such regulation, he shall issue to such manufacturer, processor, or packer an order determining that a permit shall

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be required before the food may be introduced or delivered for introduction into interstate commerce by that person. The order shall specify the mandatory conditions and requirements with which there is a lack of compliance.

(1) The manufacturer, processor, or packer shall have 3 working days after receipt of such order within which to file objections. Such objections may be filed by telegram, telex, or any other mode of written communication addressed to the Food and Drug Administration, Bureau of Foods, 200 C St. N.W., Washington, DC 20204. If such objections are filed, the determination stayed pending a hearing to be held within 5 working days after the filing of objections on the issues involved. Unless the Commissioner determines that the objections raise no genuine and substantial issue of fact to justify a hearing.

(2) If the Commissioner finds that there is an imminent hazard to health, the order shall contain this finding and the reasons therefor, and shall state that the determination of the need for a permit is effective immediately pending an expedited hearing.

(3) A hearing under this section shall be conducted by the Commissioner or his designee at a location agreed upon by the objector and the Commissioner or, if such agreement cannot be reached, at a location designated by the Commissioner. The manufacturer, processor, or packer shall have the right to cross-examine the Food and Drug Administration's witnesses and present witnesses on his own behalf.

Within 5 working days after the hearing, and based on the evidence presented at the hearing, the Commissioner shall determine whether a permit is required and shall so inform the manufacturer, processor, or packer in writing, with the reasons for his determination.

The Commissioner's determination of the need for a permit constitutes final agency action from which no appeal lies to the courts. The Commissioner will not stay a determination of need for a permit pending court action except in unusual circumstances, but will participate in expediting any such appeal.

§ 508.6 Revocation of determination of need for permit.

(a) A permit shall be required only during such temporary period as is necessary to protect the public health.

(b) Whenever the Commissioner has reason to believe that a permit holder is in compliance with the mandatory requirements and conditions established in Subpart B of this part and is likely to remain in compliance, he shall, on his own initiative or on the application of the permit holder, revoke both the determination of need for a permit and the permit that had been issued. If denied, the applicant shall, upon request, be afforded a hearing conducted in accordance with § 508.5 (b) and (c) as soon as practicable. Such revocation is without prejudice to the initiation of further permit proceedings with respect to the same manufacturer, processor, or packer should later information again show the need for a permit.

§ 508.7 Issuance or denial of permit.

(a) After a determination and notification by the Commissioner in accordance with the provisions of § 508.5 that a manufacturer, processor, or packer requires a permit, such manufacturer, processor, or packer may not thereafter introduce or deliver for introduction into interstate commerce any such food manufactured, processed, or packed by him unless he holds a permit issued by the Commissioner or obtains advance written approval of the Food and Drug Administration pursuant to § 508.12(a).

(b) Any manufacturer, processor, or packer for whom the Commissioner has made a determination that a permit is necessary may apply to the Commissioner for the issuance of such a permit. The application shall contain such data and information as is necessary to show that all mandatory requirements and conditions for the manufacture, processing, or packing of a food for which regulations are established in Subpart B of this part are met and, in particular, shall show that the deviations specified in the Commissioner's determination of the need for a permit have been corrected or suitable interim measures established.

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Within 10 working days after receipt of such application, (except that the Commissioner may extend such time an additional 10 working days where necessary), the Commissioner shall issue a permit, deny the permit, or offer the applicant a hearing conducted in accordance with § 508.5 (b) and (c) as to whether the permit should be issued. The Commissioner shall issue such a permit to which shall be attached, in addition to the mandatory requirements and conditions of Subpart B of this part, any additional requirements or conditions which may be necessary to protect the public health if he finds that all mandatory requirements and conditions of Subpart B of this part are met or suitable interim measures are established.

(c) Denial of a permit constitutes final agency action from which appeal lies to the courts. The Commissioner will not stay such denial pending court appeal except in unusual circumstances, but will participate in expediting any such appeal.

§ 508.10 Suspension and reinstatement of permit.

(a) Whenever the Commissioner finds that a permit holder is not in compliance with the mandatory requirements and conditions established by the permit, he shall immediately suspend the permit and so inform the permit holder, with the reasons for the suspension.

(b) Upon application for reinstatement of a permit, the Commissioner shall, within 10 working days, reinstate the permit if he finds that the person is in compliance with the mandatory requirements and conditions established by the permit or deny the application.

(c) Any person whose permit has been suspended or whose application for reinstatement has been denied may request a hearing. The hearing shall be conducted by the Commissioner or his designee within 5 working days of receipt of the request at a location agreed upon by the objector and the Commissioner or, if an agreement cannot be reached, at a location designated by the Commissioner. The permit holder shall have the right to present witnesses on his own behalf

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and to cross-examine the Food and Drug Administration's witnesses.

(d) Within 5 working days after the hearing, and based on the evidence presented at the hearing, the Commissioner shall determine whether the permit shall be reinstated and shall so inform the permit holder, with the reasons for his decision.

(e) Denial of an application for reinstatement of a permit constitutes final agency action from which appeal lies to the courts. The Commissioner will not stay such denial pending court appeal except in unusual circumstances, but will participate in expediting any such appeal.

§ 508.12 Manufacturing, processing, or packing without a permit or in violation of a permit.

(a) A manufacturer, processor, or packer may continue at his own risk to manufacture, process, or pack without a permit a food for which the Commissioner has determined that a permit is required. All food so manufactured, processed, or packed during such period without a permit shall be retained by the manufacturer, processor, or packer and may not be introduced or delivered for introduction into interstate commerce without the advance written approval of the Food and Drug Administration. Such approval may be granted only upon an adequate showing that such food is free from microorganisms of public health significance. The manufacturer, processor, or packer may provide to the Commissioner, for his consideration in making any such determination, an evaluation of the potential public health significance of such food by a competent authority in accordance with procedures recognized as being adequate to detect any potential hazard to public health. Within 20 working days after receipt of a written request for such written approval the Food and Drug Administration shall either issue such written approval or deny the request. If the request is denied, the applicant shall, upon request, be afforded a prompt hearing conducted in accordance with § 508.5 (b) and (c).

(b) Except as provided in paragraph (a) of this section, no manufacturer, processor, or packer may introduce or deliver for introduction into interstate commerce without a permit or in violation of a permit a food for which the Commissioner has determined that a permit is required. Where a manufacturer, processor, or packer utilizes a consolidation warehouse or other storage facility under his control, interstate shipment of any such food from the point of production to that warehouse or storage facility shall not violate this paragraph, provided that no further introduction or delivery for introduction into interstate commerce is made from that consolidated warehouse or storage facility except as provided in paragraph (a) of this section.

508.19 Establishment of requirements for exemption from section 404 of the act.

(a) Whenever the Commissioner finds after investigation that the distribution in interstate commerce of any class of food may, by reason of contamination with microorganisms during the manufacture, processing, or packing thereof in any locality, be injurious to health, and that such injurious nature cannot be adequately determined after such articles have entered interstate commerce, he shall promulgate regulations in Subpart B of this part establishing requirements and conditions governing the manufacture, processing, or packing of the food necessary to protect the public health. Such regulations may be promulgated by the Commissioner on his own initiative or in response to a petition from any interested person pursuant to Part 10 of this chapter.

(b) A manufacturer, processor, or packer of a food for which a regulation has been promulgated in Subpart B of this part shall be exempt from the requirement for a permit only if it meets all of the mandatory requirements and conditions established in the regulation.

FR 38637, Sept. 10, 1976, as amended at FR 4717, Jan. 25, 1977; 42 FR 15675, Mar. 9, 1977]

Subpart B—Requirements and Conditions for Exemption From or Compliance With an Emergency Permit

§ 508.35 Thermal processing of low-acid animal foods packaged in hermetically sealed containers.

(a) Inadequate or improper manufacture, processing, or packing of thermally processed low-acid foods in hermetically sealed containers may result in the distribution in interstate commerce of processed foods that may be injurious to health. The harmful nature of such foods cannot be adequately determined after these foods have entered into interstate commerce. The Commissioner of Food and Drugs therefore finds that, in order to protect the public health, it may be necessary to require any commercial processor, in any establishment engaged in the manufacture, processing, or packing of thermally processed low-acid foods in hermetically sealed containers, to obtain and hold a temporary emergency permit provided for under section 404 of the Federal Food, Drug, and Cosmetic Act. Such a permit may be required whenever the Commissioner finds, after investigation, that the commercial processor has failed to fulfill all the requirements of this section, including registration and the filing of process information, and the mandatory portions of Part 507 of this chapter. These requirements are intended to ensure safe manufacture, processing, and packing procedures and to permit the Food and Drug Administration to verify that these procedures are being followed. Such failure shall constitute a prima facie basis for the immediate application of the emergency permit control provisions of section 404 of the act to that establishment, pursuant to the procedures established in Subpart A of this part.

(b) The definitions in § 507.3 of this chapter are applicable when such terms are used in this section.

(c) Registration and process filing:

(1) *Registration.* A commercial processor when first engaging in the manufacture, processing, or packing of thermally processed low-acid foods in her-

metically sealed containers in any state, as defined in section 201(a)(1) of the act, shall, not later than 10 days after first so engaging, register with the Food and Drug Administration on Form FD-2541 (food canning establishment registration) information including (but not limited to) his name, principal place of business, the location of each establishment in which such processing is carried on, the processing method in terms of the type of processing equipment employed, and a list of the low-acid foods so processed in each such establishment. These forms are available from the Food and Drug Administration, Bureau of Foods, Industry Guidance Branch, HFF-326, 200 C St. SW, Washington, DC 20204, or at any Food and Drug Administration district office. The completed form shall be submitted to the Food and Drug Administration, Bureau of Foods, Division of Food Technology, HFF-419, 200 C St. SW, Washington, DC 20204. Commercial processors presently so engaged shall register not later than July 13, 1973. Commercial processors duly registered in accordance with this section shall notify the Food and Drug Administration not later than 90 days after such commercial processor ceases or discontinues the manufacture, processing, or packing of thermally processed foods in any establishment: *Provided*, That such notification shall not be required as to the temporary cessation necessitated by the seasonal character of the particular establishment's production or caused by temporary conditions including but not limited to strikes, lock-outs, fire, or acts of God.

(2) *Process filing.* A commercial processor engaged in the thermal processing of low-acid foods packaged in hermetically sealed containers shall, not later than 60 days after registration and prior to the packing of a new product, provide the Food and Drug Administration information as to the scheduled processes including but not limited to the processing method, type of retort or other thermal processing equipment employed, minimum initial temperatures, times and temperatures of processing, sterilizing value (F_0), or other equivalent scientific evidence of process adequacy, critical

cal control factors affecting heat penetration, and source and date of the establishment of the process, for each such low-acid food in each container size: *Provided*, That the filing of such information does not constitute approval of the information by the Food and Drug Administration, and that information concerning processes and other data so filed shall be regarded as trade secrets within the meaning of 21 U.S.C. 331(j) and 18 U.S.C. 1905. This information shall be submitted on the following forms as appropriate: Form FD-2541a (food canning establishment and process filing for still retort processes), form FD-2541b (food canning establishment and process filing for agitating processes), or form FD-2541c (food canning establishment and process filing for other than still retort and agitating processes). These forms are available from the Food and Drug Administration, Bureau of Foods, Industry Guidance Branch, HFF-326, 200 C St. SW, Washington, DC 20204, or at any Food and Drug Administration district office. The completed form(s) shall be submitted to the Food and Drug Administration, Bureau of Foods, Division of Food Technology, HFF-419, 200 C St. SW, Washington, DC 20204.

(i) If all the necessary information is not available for existing products, the processor shall, at the time the existing information is provided to the Food and Drug Administration request in writing an extension of time for submission of such information, specifying what additional information is to be supplied and the date by which it is to be submitted. Within 30 working days after receipt of such request the Food and Drug Administration shall either grant or deny such request in writing.

(ii) If a packer intentionally makes a change in a previously filed scheduled process by reducing the initial temperature or retort temperature, reducing the time of processing, or changing the product formulation, the container, or any other condition basic to the adequacy of scheduled process, he shall prior to using such changed process obtain substantiation by qualified scientific authority as to its adequacy. Such substantiation may be obtained

by telephone, telegram, or other media, but must be promptly recorded, verified in writing by the authority, and contained in the packer's files for review by the Food and Drug Administration. Within 30 days after first use, the packer shall submit to the Food and Drug Administration, Bureau of Foods, 200 C St. SW, HFF-419, Washington, DC 20204 a complete description of the modifications made and utilized, together with a copy of his file record showing prior substantiation by a qualified scientific authority as to the safety of the changed process. Any intentional change of a previously filed scheduled process or modification thereof in which the change consists solely of a higher initial temperature, a higher retort temperature, or a longer processing time, shall not be considered a change subject to this paragraph, but if thereafter that modification is to be regularly scheduled, the modified process shall be promptly filed as a scheduled process, accompanied by full information on the specified forms as provided in this paragraph.

(iii) Many packers employ an "operating" process in which retort operators are instructed to use retort temperatures and/or processing times slightly in excess of those specified in the scheduled process as a safety factor to compensate for minor fluctuations in temperature or time to assure that the minimum times and temperatures in the scheduled process are always met. This would not constitute a modification of the scheduled process.

(3) *Process adherence and information.* (i) A commercial processor engaged in the thermal processing of low-acid foods packaged in hermetically sealed containers in any registered establishment shall process each low-acid food in each container size in conformity with at least the scheduled processes and modifications filed pursuant to paragraph (c)(2) of this section.

(ii) *Process information availability:* When requested by the Food and Drug Administration in writing, a commercial processor engaged in thermal processing of low-acid foods packaged in hermetically sealed containers shall

provide the Food and Drug Administration with any information concerning processes and procedures which is deemed necessary by the Food and Drug Administration to determine the adequacy of the process: *Provided*, That the furnishing of such information does not constitute approval of the information by the Food and Drug Administration, and that the information concerning processes and other data so furnished shall be regarded as trade secrets within the meaning of 21 U.S.C. 331(j) and 18 U.S.C. 1905.

(d) A commercial processor engaged in the thermal processing of low-acid foods packaged in hermetically sealed containers shall promptly report to the Food and Drug Administration any instance of spoilage or process deviation the nature of which indicates potential health significance where any lot of such food has in whole or in part entered distribution.

(e) A commercial processor engaged in thermal processing of low-acid foods packaged in hermetically sealed containers shall promptly report to the Food and Drug Administration any instance wherein any lot of such food, which may be injurious to health by reason of contamination with microorganisms, has in whole or in part entered distribution.

(f) A commercial processor engaged in the thermal processing of low-acid foods packaged in hermetically sealed containers shall have prepared and in his files a current procedure which he will use for products under his control and which he will ask his distributor to follow, including plans for effecting recalls of any product that may be injurious to health; for identifying, collecting, warehousing, and controlling the product; for determining the effectiveness of such recall; for notifying the Food and Drug Administration of any such recall; and for implementing such recall program.

(g) All operators of retorts, thermal processing systems, aseptic processing and packaging systems, or other thermal processing systems, and container closure inspectors shall be under the operating supervision of a person who has attended a school approved by the Commissioner for giving instruction in retort operations, aseptic processing

and packaging systems operations or other thermal processing systems operations, and container closure inspections, and has satisfactorily completed the prescribed course of instruction: *Provided*, That this requirement shall not apply in the State of California as listed in paragraph (j) of this section and shall not apply until March 25, 1975 in any other State. The Commissioner will not withhold approval of any school qualified to give such instruction.

(h) A commercial processor engaged in the thermal processing of low-acid foods packaged in hermetically sealed containers shall prepare, review, and retain at the processing plant for a period of not less than 1 year, and at the processing plant or other reasonably accessible location for an additional 2 years, all records of processing, deviations in processing, container closure inspections, and other records specified in Part 507 of this chapter. If during the first year of the 3-year record retention period the processing plant is closed for a prolonged period between seasonal packs, the records may be transferred to some other reasonably accessible location at the end of the seasonal pack. Upon written demand during the course of a factory inspection pursuant to section 704 of the act by a duly authorized employee of the Food and Drug Administration, a commercial processor shall permit the inspection and copying by such employee of these records to verify the adequacy of processing, the integrity of container closures, and the coding of the products.

(i) This section shall not apply to the commercial processing of any food processed under the continuous inspection of the meat and poultry inspection program of the Animal and Plant Health Inspection Service of the Department of Agriculture under the Federal Meat Inspection Act (34 Stat. 1256, as amended by 81 Stat. 584 (21 U.S.C. 601 et seq.)) and the Poultry Products Inspection Act (71 Stat. 441, as amended by 82 Stat. 791; 21 U.S.C. 451 et seq.).

(j) Compliance with State regulations: (1) Wherever the Commissioner finds that any State regulates the commercial thermal processing of low-

acid foods in accordance with effective regulations specifying at least the requirements of Part 507 of this chapter, he shall issue a notice stating that compliance with such State regulations shall constitute compliance with Part 507 of this chapter. However, the provisions of this section shall remain applicable to the commercial processing of low-acid foods in any such State, except that, either the State through its regulatory agency or each processor of low-acid foods in such State shall file with the Bureau of Foods the registration information and the processing information prescribed in paragraph (c) of this section.

(2) The Commissioner finds that the regulations adopted by the State of California under the laws relating to cannery inspections governing thermal processing of low-acid foods packaged in hermetically sealed containers satisfy the requirements of Part 507 of this chapter.

Accordingly, processors, who under the laws relating to cannery inspections are licensed by the State of California and who comply with such state regulations, shall be deemed to comply with the requirements of Part 507 of this chapter.

(k) Imports: (1) This section shall apply to any foreign commercial processor engaged in the thermal processing of low-acid foods packaged in hermetically sealed containers and offering such foods for import into the United States except that, in lieu of providing for the issuance of an emergency permit under paragraph (a) of this section, the Commissioner will request the Secretary of the Treasury to refuse admission into the United States, pursuant to section 801 of the act, of any such low-acid foods which the Commissioner determines, after investigation, may result in the distribution in interstate commerce of processed foods that may be injurious to health as set forth in paragraph (a) of this section.

(2) Any such food refused admission shall not be admitted until such time as the Commissioner may determine that the commercial processor offering the food for import is in compli-

ance with the requirements and conditions of this section and that such food is not injurious to health. For the purpose of making such determination, the Commissioner reserves the right for a duly authorized employee of the Food and Drug Administration to inspect the commercial processor's manufacturing, processing, and packing facilities.

(1) The following data and information submitted to the Food and Drug Administration pursuant to this section are not available for public disclosure unless they have been previously disclosed to the public as defined in § 20.81 of this chapter or they relate to a product or ingredient that has been abandoned and they no longer represent a trade secret or confidential commercial or financial information as defined in § 80.61 of this chapter:

(1) Manufacturing methods or processes, including quality control information.

(2) Production, sales, distribution, and similar data and information, except that any compilation of such data and information aggregated and prepared in a way that does not reveal data or information which is not available for public disclosure under this provision is available for public disclosure.

(3) Quantitative or semiquantitative formulas.

(41 FR 38637, Sept. 10, 1976, as amended at 42 FR 15675, Mar. 22, 1977)

PART 509—UNAVOIDABLE CONTAMINANTS IN ANIMAL FOOD AND FOOD-PACKAGING MATERIAL

Subpart A—General Provisions

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- 509.3 Definitions and interpretations.
 - 509.4 Establishment of regulations.
 - 509.5 Petitions.
 - 509.6 Added poisonous or deleterious substances.
 - 509.7 Unavoidability.
 - 509.8 Exemptions.
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Sec.

Subpart B—Tolerances for Unavoidable Poisonous or Deleterious Substances

509.30 Temporary tolerances for polychlorinated biphenyls (PCB's).

Subpart C—Naturally Occurring Poisonous or Deleterious Substances [Reserved]

AUTHORITY: Secs. 306, 402(a), 406, 408, 409, 701, 52 Stat. 1045-1046 as amended, 1049 as amended, 1055-1056 as amended; 68 Stat. 511-518 as amended; 72 Stat. 1785-1788 as amended (21 U.S.C. 336, 342(a), 346, 346a, 348, 371).

SOURCE: 42 FR 52821, Sept. 30, 1977, unless otherwise noted.

Subpart A—General Provisions

§ 509.3 Definitions and interpretations.

(a) "Act" means the Federal Food, Drug, and Cosmetic Act.

(b) The definitions of terms contained in section 201 of the act are applicable to such terms when used in this part unless modified in this section.

(c) A "naturally occurring poisonous or deleterious substance" is a poisonous or deleterious substance that is an inherent natural constituent of a food and is not the result of environmental, agricultural, industrial, or other contamination.

(d) An "added poisonous or deleterious substance" is a poisonous or deleterious substance that is not a naturally occurring poisonous or deleterious substance. When a naturally occurring poisonous or deleterious substance is increased to abnormal levels through mishandling or other intervening acts, it is an added poisonous or deleterious substance to the extent of such increase.

(e) "Food" includes pet food, animal feed, and substances migrating to food from food-contact articles.

§ 509.4 Establishment of regulations.

(a) When appropriate under the criteria of § 509.6, a tolerance for an added poisonous or deleterious substance, which may be a food additive, may be established by regulation in Subpart B of this part under the provisions of section 406 of the act. A tol-

erance may prohibit any detectable amount of the substance in food.

(b)(1) When appropriate under the criteria of § 509.6, an action level for an added poisonous or deleterious substance, which may be a food additive, may be established to define the level of contamination at which a food will be deemed to be adulterated. An action level may prohibit any detectable amount of the substance in food.

(2) Whenever an action level is established, a notice shall be published in the FEDERAL REGISTER as soon as practicable thereafter. The notice shall call attention to the material supporting the action level which shall be on file with the Dockets Management Branch before the notice is published. The notice shall invite public comment on the action level. Regulatory action may be taken at any time after an action level is established, and need not await publication of the notice. An action level may be changed at any time if the protection of the public health so requires. A notice shall be published in the FEDERAL REGISTER as soon as practicable after an action level is changed.

(c) A regulation may be established in Subpart C of this part to identify a food containing a naturally occurring poisonous or deleterious substance which will be deemed to be adulterated under section 402(a)(1) of the act. These regulations do not constitute a complete list of such foods.

§ 509.5 Petitions.

The Commissioner of Food and Drugs, either on his own initiative or on behalf of any interested person who has submitted a petition, may issue a proposal to establish, revoke, or amend a regulation under this part. Any such petition shall include an adequate factual basis to support the petition, shall be in the form set forth in § 10.65 of this chapter, and will be published in the FEDERAL REGISTER for comment if it contains reasonable grounds for the proposed regulation.

§ 509.6 Added poisonous or deleterious substances.

(a) Use of an added poisonous or deleterious substance, other than a pesticide chemical, that is also a food addi-

tive will be controlled by a regulation issued under section 409 of the act when possible. When such a use cannot be approved under the criteria of section 409, or when the added poisonous or deleterious substance is not a food additive, a tolerance or action level may be established pursuant to the criteria established in paragraphs (b) and (c) of this section. Residues resulting from the use of an added poisonous or deleterious substance that is also a pesticide chemical will ordinarily be controlled by a tolerance established in a regulation issued under section 406, 408, or 409 by the U.S. Environmental Protection Agency (EPA). When such a regulation has not been issued, an action level for an added poisonous or deleterious substance that is also a pesticide chemical may be established by the Food and Drug Administration. The Food and Drug Administration will request EPA to recommend such an action level pursuant to the criteria established in paragraph (c) of this section.

(b) A tolerance for an added poisonous or deleterious substance in any food may be established when the following criteria are met:

(1) The substance cannot be avoided by good manufacturing practice.

(2) The tolerance established is sufficient for the protection of the public health, taking into account the extent of which the presence of the substance cannot be avoided and the other ways in which the consumer may be affected by the same or related poisonous or deleterious substances.

(3) No technological or other changes are foreseeable in the near future that might affect the appropriateness of the tolerance established. Examples of changes that might affect the appropriateness of the tolerance include anticipated improvements in good manufacturing practice that would change the extent to which use of the substance is unavoidable and anticipated studies expected to provide significant new toxicological or use data.

(c) An action level for an added poisonous or deleterious substance in any food may be established when the criteria in paragraph (b) of this section are met, except that technological or

other changes that might affect the appropriateness of the tolerance are foreseeable in the near future. An action level shall cease to be enforced and shall be revoked when a tolerance for the same substance and use has become effective.

(d) Tolerances will be established under authority appropriate for action levels (sections 306, 402(a), and 701(a) of the act, together with section 408 or 409 if appropriate) as well as under authority appropriate for tolerances (sections 406 and 701 of the act). In the event the effectiveness of a tolerance is stayed pursuant to section 701(e)(2) of the act by the filing of an objection, the order establishing the tolerance shall be deemed to be an order establishing an action level until final action is taken upon such objection.

§ 509.7 Unavoidability.

(a) Tolerances and action levels in this part are established at levels based on the unavoidability of the poisonous or deleterious substance concerned and do not establish a permissible level of contamination where it is avoidable.

(b) Compliance with tolerances and action levels does not excuse failure to observe either the requirement in section 402(a)(4) of the Federal Food, Drug, and Cosmetic Act that food may not be prepared, packed, or held under insanitary conditions or the other requirements in this chapter that food manufacturers must observe current good manufacturing practices. Evidence obtained through factory inspection or otherwise indicating such a violation renders the food unlawful, even though the amounts of poisonous or deleterious substances are lower than the currently established tolerances or action levels. The manufacturer of food must at all times utilize quality control procedures which will reduce contamination to the lowest level currently feasible.

§ 509.8 Exemptions.

(a) The Commissioner may exempt from regulatory action and permit the marketing of any food that is unlawfully contaminated with a poisonous or deleterious substance if:

(1) He determines (i) based upon all available scientific evidence, that the food is safe for consumption, and (ii) that destruction or diversion of the food involved would result in a substantial adverse impact on the national food supply.

(2) Such determination is published as a notice in the **FEDERAL REGISTER** and public comment shall be invited on the determination. The notice shall call attention to the material supporting the determination, which shall be on file with the Dockets Management Branch before the notice is published.

(3) The determination identifies the level of contamination allowed by the exemption, and the food to which it applies, e.g., the specific growing area or other identifying information. The exemption shall not apply to any other food produced in any other area or at any other time. Contaminated food not subject to the exemption will remain subject to regulatory action.

(b) Any person responsible for contamination of the food involved, or shipment of any such food in interstate commerce prior to the issuance of an exemption pursuant to this section, shall remain subject to regulatory action pursuant to sections 302 (injunction proceedings) and 303 (penalties) of the act.

(c) In the case of a poisonous or deleterious substance which is a pesticide chemical, the level of contamination allowed by the exemption shall, upon request of the Food and Drug Administration, be specified by the Environmental Protection Agency pursuant to paragraph (a)(1)(i) of this section and promulgated by the Commissioner. No exemption for a pesticide chemical shall be promulgated without the concurrence of the Environmental Protection Agency.

§ 509.15 Use of polychlorinated biphenyls (PCB's) in establishments manufacturing food-packaging materials.

(a) Polychlorinated biphenyls (PCB's) represent a class of toxic industrial chemicals manufactured and sold under a variety of trade names, including: Aroclor (United States); Phenoclor (France); Colphen (Germany); and Kanaclor (Japan). PCB's are

highly stable, heat resistant, and non-flammable chemicals. Industrial uses of PCB's include, or did include in the past, their use as electrical transformer and capacitor fluids, heat transfer fluids, hydraulic fluids, and plasticizers, and in formulations of lubricants, coatings, and inks. Their unique physical and chemical properties and widespread, uncontrolled industrial applications have caused PCB's to be a persistent and ubiquitous contaminant in the environment, causing the contamination of certain foods. In addition, incidents have occurred in which PCB's have directly contaminated animal feeds as a result of industrial accidents (leakage or spillage of PCB fluids from plant equipment). These accidents in turn caused the contamination of food products intended for human consumption (meat, milk and eggs). Investigations by the Food and Drug Administration have revealed that a significant percentage of paper food-packaging material contains PCB's which can migrate to the packaged food. The origin of PCB's in such material is not fully understood. Recycled fibers containing carbonless copy paper (contains 3 to 5 percent PCB's) have been identified as a primary source of PCB's in paper products. Some virgin paper products have also been found to contain PCB's, the source of which is generally attributed to direct contamination from industrial accidents from the use of PCB-containing equipment and machinery in food-packaging manufacturing establishments. Since PCB's are toxic chemicals, the PCB contamination of food-packaging materials as a result of industrial accidents, which can cause the PCB contamination of food, represents a hazard to public health. It is therefore necessary to place certain restrictions on the industrial uses of PCB's in establishments manufacturing food-packaging materials.

(b) The following special provisions are necessary to preclude the accidental PCB contamination of food-packaging materials:

(1) New equipment or machinery for manufacturing food-packaging materials shall not contain or use PCB's.

(2) On or before September 4, 1973, the management of establishments

manufacturing food-packaging materials shall:

(i) Have the heat exchange fluid used in existing equipment for manufacturing food-packaging materials sampled and tested to determine whether it contains PCB's or verify the absence of PCB's in such formulations by other appropriate means. On or before Sept. 4, 1973, any such fluid formulated with PCB's must to the fullest extent possible commensurate with current good manufacturing practices be replaced with a heat exchange fluid that does not contain PCB's.

(ii) Eliminate to the fullest extent possible commensurate with current good manufacturing practices from the establishment any other PCB-containing equipment, machinery and materials wherever there is a reasonable expectation that such articles could cause food-packaging materials to become contaminated with PCB's either as a result of normal use or as a result of accident, breakage, or other mishap.

(iii) The toxicity and other characteristics of fluids selected as PCB replacements must be adequately determined so that the least potentially hazardous replacement is used. In making this determination with respect to a given fluid, consideration should be given to (a) its toxicity; (b) the maximum quantity that could be spilled onto a given quantity of food before it would be noticed, taking into account its color and odor; (c) possible signaling devices in the equipment to indicate a loss of fluid, etc.; and (d) its environmental stability and tendency to survive and be concentrated through the food chain. The judgment as to whether a replacement fluid is sufficiently non-hazardous is to be made on an individual installation and operation basis.

(c) The provisions of this section do not apply to electrical transformers and condensers containing PCB's in sealed containers.

Subpart B—Tolerances for Unavoidable Poisonous or Deleterious Substances

§ 509.30 Temporary tolerances for polychlorinated biphenyls (PCB's).

(a) Polychlorinated biphenyls (PCB's) are toxic, industrial chemicals. Because of their widespread, uncontrolled industrial applications, PCB's have become a persistent and ubiquitous contaminant in the environment. As a result, certain foods and animal feeds, principally those of animal and marine origin, contain PCB's as unavoidable, environmental contaminants. PCB's are transmitted to the food portion (meat, milk, and eggs) of food producing animals ingesting PCB contaminated animal feed. In addition, a significant percentage of paper food-packaging materials contain PCB's which may migrate to the packaged food. The source of PCB's in paper food-packaging materials is primarily of certain types of carbonless copy paper (containing 3 to 5 percent PCB's) in waste paper stocks used for manufacturing recycled paper. Therefore, temporary tolerances for residues of PCB's as unavoidable environmental or industrial contaminants are established for a sufficient period of time following the effective date of this paragraph to permit the elimination of such contaminants at the earliest practicable time. For the purposes of this paragraph, the term "polychlorinated biphenyls (PCB's)" is applicable to mixtures of chlorinated biphenyl compounds, irrespective of which mixture of PCB's is present as the residue. The temporary tolerances for residues of PCB's are as follows:

(1) 0.2 part per million in finished animal feed for food-producing animals (except the following finished animal feeds: feed concentrates, feed supplements, and feed premixes).

(2) 2 parts per million in animal feed components of animal origin, including fishmeal and other by-products of marine origin and in finished animal feed concentrates, supplements, and premixes intended for food-producing animals.

(3) 10 parts per million in paper food-packaging material intended for or used with finished animal feed and

any components intended for animal feeds. The tolerance shall not apply to paper food-packaging material separated from the food therein by a functional barrier which is impermeable to migration of PCB's.

(b) A compilation entitled "Analytical Methodology for Polychlorinated Biphenyls, February 1973" for determining compliance with the tolerances established in this section is available from the Dockets Management Branch, Food and Drug Administration, Room 4-62, Parklawn Building, 5600 Fishers Lane, Rockville, MD 20857.

NOTE: At 38 FR 22794, Aug. 24, 1973, the following appeared concerning § 509.30(a)(9) (formerly § 122.10(a)(9)):

• • • § 509.30(a)(9) is hereby stayed pending full review of the objections and requests for hearing. • • •

In the interim, as stated in the final order (38 FR 18098) the Food and Drug Administration will enforce the temporary tolerance level established by § 509.30(a)(9) by seizing any paper food-packaging material shipped in interstate commerce after September 4, 1973 containing higher than the specified level of PCB's as adulterated in violation of sec. 402 of the act.

[42 FR 52821, Sept. 30, 1977, as amended at 46 FR 8460, Jan. 27, 1981]

Subpart C—Naturally Occurring Poisonous or Deleterious Substances [Reserved]

PART 510—NEW ANIMAL DRUGS

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510.410 Corticosteroids for oral, injectable, and ophthalmic use in animals; warnings and labeling requirements.

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510.440 Injectable iron preparations.

510.450 Sulfonamide-containing drugs for oral, injectable, intramammary, or intrauterine use in food-producing animals.

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Subpart F—Animal Use Exemptions from Certification and Labeling Requirements

510.510 Antibiotic drugs for use in medicated animal feed (antibiotic medicated feed premixes).

510.515 Animal feeds bearing or containing new animal drugs subject to the provisions of section 512(n) of the act.

510.520 Exemption from batch certification requirements for antibiotic drugs for animal use subject to section 512(n) of the act.

510.521 Conditions on the effectiveness of exemptions of antibiotic drugs for animal use from batch certification requirements.

Subpart G—Sponsors of Approved Applications

510.600 Names, addresses, and drug labeler codes of sponsors of approved applications.

AUTHORITY: Secs. 512, 701(a) (21 U.S.C. 360b, 371(a)); 21 CFR 5.10 and 5.83, unless otherwise noted.

SOURCE: 40 FR 13807, Mar. 27, 1975, unless otherwise noted.

Subpart A—General Provisions

§ 510.3 Definitions and interpretations.

As used in this part:

(a) The term "act" means the Federal Food, Drug, and Cosmetic Act, as amended (secs. 201-902, 52 Stat. 1040 et seq., as amended; 21 U.S.C. 321-392).

(b) "Department" means the Department of Health and Human Services.

(c) "Secretary" means the Secretary of Health and Human Services.

(d) "Commissioner" means the Commissioner of Food and Drugs.

(e) "Person" means individuals, partnerships, corporations, and associations.

(f) The definitions and interpretations of terms contained in section 201 of the act shall be applicable to such terms when used in the regulations in this part.

(g) The term "new animal drug" means any drug intended for use for animals other than man, including any drug intended for use in animal feed but not including such animal feed:

(1) The composition of which is such that such drug is not generally recognized, among experts qualified by sci-

entific training and experience to evaluate the safety and effectiveness of animal drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof; except that such a drug not so recognized shall not be deemed to be a "new animal drug" if at any time prior to June 25, 1938, it was subject to the Food and Drug Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use; or

(2) The composition of which is such that such drug, as a result of investigations to determine its safety and effectiveness for use under such conditions, has become so recognized but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions; or

(3) Which drug is composed wholly or partly of any kind of penicillin, streptomycin, chlortetracycline, chloramphenicol, or bacitracin, or any derivative thereof, except when there is in effect a published order of the Secretary declaring such drug not to be a new animal drug on the grounds that:

(i) The requirement of certification of batches of such drug, as provided for in section 512(n) of the act, it is not necessary to insure that the objectives specified in paragraph (3) thereof are achieved; and

(ii) That neither paragraph (g) (1) nor (2) of this section applies to such drug.

(h) The term "animal feed" means an article which is intended for use for food for animals other than man and which is intended for use as a substantial source of nutrients in the diet of the animal, and is not limited to a mixture intended to be the sole ration of the animal.

(i) The newness of an animal drug, including a new animal drug intended for use in or on animal feed, may arise by reason of: (1) The newness for its intended drug use of any substance of which the drug is comprised, in whole or in part, whether it be an active substance or a menstruum, excipient, carrier, coating, or other component; (2) the newness for its intended drug use of a combination of two or more sub-

stances, none of which is itself a new animal drug; (3) the newness for its intended drug use of the proportion of a substance in a combination, even though such combination containing such substance in other proportion is not a new animal drug; (4) the newness for its intended drug use in a different species of animal; (5) the newness of its intended drug use in diagnosing, curing, mitigating, treating, or preventing a disease, or to affect a structure or function of the animal body, even though such drug is not a new animal drug when used in another disease or to affect another structure or function of the body; or (6) the newness of a dosage, or method or duration of administration or application, or any other condition of use prescribed, recommended, or suggested in the labeling of such drug, even though such drug or animal feed containing such drug when used in another dosage, or another method or duration of administration or application, or different condition, is not a new animal drug.

(j) "Animals used only for laboratory research" and "laboratory research animals" mean individual animals or groups of animals intended for use and used solely for laboratory research purposes, regardless of species, and does not include animals intended to be used for any food purposes or animals intended to be kept as livestock.

(k) The term "sponsor" means the person responsible for an investigation of a new animal drug, including responsibility for compliance with applicable provisions of the act and regulations. The "sponsor" may be an individual, partnership, corporation, or Government agency or may be a manufacturer, scientific institution, or an investigator regularly and lawfully engaged in the investigation of new animal drugs.

(l) "Designated journal(s)" means journals listed in § 510.95.

(Secs. 409, 501, 502, 503, 505, 506, 507, 512-516, 520, 701, 706, 52 Stat. 1049-1053 as amended, 1055, 1056 as amended, 55 Stat. 851, 59 Stat. 463 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 599-407 as amended, 82 Stat. 343-351, 90 Stat. 540-560 (21 U.S.C. 348, 351, 352, 353, 355, 356, 357, 360b-360f, 371, 370); secs. 215, 301, 351, 354-360F,

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58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 241, 262, 263b-236n))

[40 FR 13807, Mar. 27, 1975, as amended at 50 FR 7517, Feb. 22, 1985]

§ 510.4 Biologics; products subject to license control.

An animal drug produced and distributed in full conformance with the animal virus, serum, and toxin law of March 4, 1913 (37 Stat. 832; 21 U.S.C. 151 et seq.) and any regulations issued thereunder shall not be deemed to be subject to section 512 of the Federal Food, Drug, and Cosmetic Act.

§ 510.5 Certification of new animal drugs containing any kind of penicillin, streptomycin, chlortetracycline, chloramphenicol, or bacitracin, or derivative thereof.

(a) *New animal drugs subject to the provisions of section 512(n) of the act.* New animal drugs that contain or purport to contain any kind of penicillin, streptomycin, chlortetracycline, chloramphenicol, bacitracin, or derivative thereof shall conform to:

(1) The specifications included in applicable monographs published pursuant to section 512(n) of the act, and

(2) The conditions of use specified in regulations published pursuant to section 512(i) of the act.

(b) *New animal drugs subject to the provisions of section 512(n) of the act and intended for use as components of animal feed.* Penicillin, streptomycin, chlortetracycline, bacitracin, feed grade bacitracin, feed grade manganese bacitracin, feed grade zinc bacitracin, and bacitracin methylene disalicylate intended for use solely in the manufacture of one or more of the medicated animal feeds described in Part 558 of this chapter, and conspicuously so labeled, shall be exempt from the certification requirements of section 512(n) of the act if its manufacturer, packer, or distributor:

(1) Holds an approval for such a drug as published in accordance with section 512(i) of the act; and

(2) Holds an effective permit from the Commissioner issued under the provisions of § 433.13 of this chapter authorizing shipment for manufacturing use to such establishment.

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(c) *Animal feeds subject to the provisions of section 512(m) of the act and bearing or containing a new animal drug subject to the provisions of section 512 (n).* An animal feed that bears or contains or purports to bear or contain penicillin, streptomycin, chlortetracycline, or bacitracin, or any derivative thereof, shall be exempted from the requirements of section 512(m) of the act in accordance with the conditions specified in applicable regulations published in Part 558 of this chapter.

§ 510.6 New animal drugs; transitional provisions re section 512 of the act.

(a) Section 512 of the Federal Food, Drug, and Cosmetic Act was enacted on June 13, 1968, to become effective August 1, 1969, by the Animal Drug Amendments of 1968 (Pub. L. 90-399).

(b) The provisions of the Animal Drug Amendments of 1968 required extensive revisions to existing regulations.

(c) Such regulations will be published at an early date in the FEDERAL REGISTER. An opportunity for comment by interested parties will be provided.

(d) Pending promulgation of the necessary regulations under section 512 of the act, the currently used Form FD 356-Rev. 1965, Form 5, and Form FD-1800 will be acceptable as a basis for approval of applications of new animal drugs and feeds containing new animal drugs under the provisions of section 512 provided that such applications include:

(1) A practicable method of analysis for determining the quantity, if any, of any substance in or on food resulting from the use of a new animal drug.

(2) The conditions and indications for use of the new animal drug, including any proposed tolerance or withdrawal period or other use restrictions for such drug required in order to assure that the proposed use of the drug will be safe, and if the new animal drug is intended for use in animal feed, appropriate purposes and conditions of use (including special labeling requirements applicable to any animal feed in which the drug is to be approved).

(3) Applications submitted in the Form FDA 1900 shall in lieu of the information required by section I include a reference to the regulation in this Subchapter E upon which the application relies as a basis for approval of the application with respect to the use of a new animal drug in feed and the name and address of the supplier of the new animal drug.

(e) A new animal drug intended for use in the manufacture of animal feed shall be deemed to be unsafe unless at the time of its removal from the establishment of a manufacturer, packer, or distributor of such drug, such manufacturer, packer, or distributor has an unrevoked written statement from the consignee of such drug or a notice from the Food and Drug Administration to the effect that with respect to the use of such drug in animal feed, the consignee:

(1) Is the holder of an approved Form FDA 1900; or

(2) Will, if the consignee is not a user of the drug, ship such drug only to a holder of an approved Form FDA 1900.

An unrevoked written notice that a new-drug application, supplemental new-drug application, antibiotic Form 10, or Form FDA 1900 has been approved for such use of the drug in animal feed meets this requirement.

(f) The requirements of section 512 of the act shall apply with regard to approval, refusal to approve, and revocation of applications with respect to new animal drugs and feeds containing new animal drugs. All prior approvals of new-drug applications, supplemental new-drug applications, master files, Form FDA 1900, and antibiotic Forms 5, 6, and 10, and food additive regulations for such drugs and feeds containing such drugs shall remain in effect until withdrawn or suspended under provisions of section 512 of the act.

[40 FR 13807, Mar. 27, 1975, as amended at 41 FR 11011, Mar. 15, 1976; 42 FR 14091, Mar. 15, 1977; 51 FR 7391, Mar. 3, 1986]

§ 510.7 Consignees of new animal drugs for use in the manufacture of animal feed.

(a) A new animal drug intended for use in the manufacture of animal feed

shall be deemed to be unsafe unless at the time of its removal from the establishment of a manufacturer, packer, or distributor of such drug, such manufacturer, packer, or distributor has an unrevoked written statement from the consignee of such drug, or a notice from the Secretary, to the effect that with respect to the use of such drug in animal feed the consignee:

(1) Is the holder of an approved application under § 514.2 of this chapter; or

(2) Will, if the consignee is not a user of the drug, ship such drug only to a holder of an approved application under § 514.2 of this chapter.

(b) The requirements of paragraph (a) of this section do not apply:

(1) Where such drugs are intended for export and/or

(2) When the use of such drug in the manufacture of a finished feed has been exempted from the requirements of section 512(m) of the act under the conditions specified by regulations published in Part 558 of this chapter.

§ 510.45 Packaging requirements for drugs for animal use.

The packaging requirements for antibiotic drugs for veterinary use are described under § 432.1 of this chapter, except that antibiotic drugs for veterinary use need not be packaged for dispensing in containers of colorless, transparent glass.

§ 510.55 Labeling requirements for antibiotic drugs for animal use.

If an antibiotic drug is subject to section 512(n) of the act and packaged for dispensing:

(a) It shall be labeled in accordance with the requirements prescribed by § 201.105 of this chapter and each package shall include information containing directions and warnings adequate for the veterinary use of the drug by the laity in lieu of the statement "Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian" (as provided in § 201.105(b)(1) of this chapter) unless such statement is required by regulations issued under section 512(i) of the act.

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(b) Its labeling shall bear any additional information required for the drug by specific regulations.

(c) Each package shall bear on its outside wrapper or container and the immediate container an expiration date prescribed for the drug as provided in § 432.5(a)(3) of this chapter with the exception provided in § 432.5(c) of this chapter.

(d) If it is intended for udder instillation in cattle, it shall be exempt from the requirements of § 201.105(b)(5) of this chapter.

(Sec. 507, 59 Stat. 468 as amended (21 U.S.C. 357))

§ 510.95 Designated journals.

The following journals are available to the Food and Drug Administration and thus permit waiving of the submission of reprints and summaries covering reports contained in these journals to the extent that such requirements are waived in the regulations in this part:

All Pet's Magazine (Jersey City).
American Journal of Veterinary Research (Chicago).
Animal Health (Journal of the Animal Health Trust) (London).
Animal Nutrition & Health (Sausalito, Calif.).
Animal Production (Edinburgh).
Avian Diseases (Amherst).
British Poultry Science (Edinburgh).
Canadian Journal of Comparative Medicine and Veterinary Science (Gardenvale, Quebec).
Canadian Veterinary Journal (Guelph, Ontario).
Cornell Veterinarian (Ithaca).
Experimental Parasitology (New York).
The Feed Bag (Milwaukee).
Feedstuffs (Minneapolis).
Hoard's Dairymen (Fort Atkinson).
Journal of the American Veterinary Medical Association (Chicago).
Journal of Animal Science (Albany).
Journal of Dairy Science (Champaign).
Journal of Economic Entomology (Baltimore).
Journal of Small Animal Practice (London).
Modern Veterinary Practice (formerly North American Veterinarian) (Wheaton, Ill.).
National Hog Farmer (Grundy Center, Iowa).
New Zealand Veterinary Journal (Wellington).
Poultry Science (Guelph, Ontario).
Praktische Tierarzt (Postfach, Germany).

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Research in Veterinary Science (Chicago).
Small Animal Clinician (Kansas City, Mo.).
Veterinaermedizin (Konstanz, Germany).
Veterinarian (London).
Veterinarian (International) (New York).
The Veterinary Bulletin (Farnham Royal, England).
Veterinary Medicine (Kansas City, Mo.).
Veterinary Record (Croydon, England).
Zentralblatt Fuer Veterinaermedizin Zentr. Veterinaermed (Berlin).

(Secs. 409, 501, 502, 503, 505, 506, 507, 512-516, 520, 701, 706, 52 Stat. 1049-1053 as amended, 1055, 1056 as amended, 55 Stat. 851, 59 Stat. 463 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 399-407 as amended, 82 Stat. 343-351, 90 Stat. 540-560 (21 U.S.C. 348, 351, 352, 353, 355, 356, 357, 360b-360f, 371, 376); secs. 215, 301, 351, 354-360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 241, 262, 263b-236n))

[40 FR 13807, Mar. 27, 1975, as amended at 50 FR 7517, Feb. 22, 1985]

Subpart B—Specific Administrative Rulings and Decisions

§ 510.105 Labeling of drugs for use in milk-producing animals.

(a) Part 540 of this chapter provides for new animal drugs intended for intramammary use in animals and includes conditions of use intended to prevent the contamination of milk from the use of such drugs.

(b) Preparations containing antibiotics and other potent drugs labeled with directions for use in milk-producing animals will be misbranded under section 502(f)(2) of the act unless their labeling bears appropriate warnings and directions for use to avoid adulteration of milk under section 402(a)(2)(D) of the act.

(c) It is the position of the Food and Drug Administration that the labeling for such preparations should bear a clear warning that either:

(1) The article should not be administered to animals producing milk, since to do so would result in contamination of the milk; or

(2) The label should bear the warning, "Milk that has been taken from animals during treatment and within _____ hours (_____ milkings) after the latest treatment must not be used for food," the blanks to be filled in with the number of hours (not to exceed

96) and milkings that the manufacturer has determined by appropriate investigation is needed to insure that the milk will not carry residues resulting from use of the preparation. If the use of the preparation as recommended does not result in contamination of the milk, neither of the above warning statements is required.

§ 510.106 Labeling of antibiotic and antibiotic-containing drugs intended for use in milk-producing animals.

Whenever the labeling of an antibiotic drug included in the regulations in this chapter suggests or recommends its use in milk-producing animals, the label of such drugs shall bear either the statement "Warning: Not for use in animals producing milk, since this use will result in contamination of the milk" or the statement "Warning: Milk that has been taken from animals during treatment and for — hours (— milkings) after the latest treatment must not be used for food", the first blank being filled in with the figure, which shall not be greater than 96, that the Commissioner has authorized the manufacturer of the drug to use, and the second figure shall be the first number divided by 12. The Commissioner shall determine what such figures shall be from information submitted by the manufacturer and which the Commissioner considers is adequate to prove that period of time after the latest treatment that the milk from treated animals will contain no residues from use of the preparation. If the Commissioner determines from the information submitted that the use of the antibiotic drug as recommended does not result in its appearance in the milk, he may exempt the drug from bearing either of the above warning statements.

Sec. 507, 59 Stat. 463 as amended (21 U.S.C. 87)

510.110 Antibiotics used in food-producing animals.

(a) The Food and Drug Administration in the interest of fulfilling its responsibilities with regard to protection of the public health has requested an evaluation of the public health aspects of the use of antibiotics in veterinary medical and nonmedical uses. There is

particular concern with regard to the potential hazards associated with the extensive use of antibiotics administered to food-producing animals. Accordingly, an ad hoc committee on the Veterinary Medical and Nonmedical Uses of Antibiotics was established by the Food and Drug Administration to study and advise the Commissioner of Food and Drugs on the uses of antibiotics in veterinary medicine and for various nonmedical purposes as such uses may affect the enforcement of the Federal Food, Drug, and Cosmetic Act with respect to their safety and effectiveness.

(b) Based upon an evaluation of the conclusions of said Committee and other relevant material, § 510.112 was published in the FEDERAL REGISTER of August 23, 1966 (31 FR 11141), asking sponsors of drugs containing any antibiotic intended for use in food-producing animals to submit data to establish whether such antibiotic and its metabolites are present as residues in edible tissues, milk, and eggs from treated animals. The data on the residues of antibiotics in milk from intramammary infusion preparations were requested within 60 days and the data on all other products were requested within 180 days following the date of publication of § 510.112 in the FEDERAL REGISTER.

(c) An evaluation of the data now available shows that use of many antibiotic preparations cause residues in edible products of treated animals for varying and, in some cases, for long periods of time following the last administration. Because of the accumulation of new information with regard to the development of resistance of bacteria to antibiotics, the ability of bacteria to transfer this resistance, and the development of sensitivity to antibiotics in humans, unauthorized and unsafe residues of antibiotics cannot be permitted in food obtained from treated animals.

(d) Based on evaluation of information available, including the conclusions of the aforementioned ad hoc Committee, the Commissioner concludes that antibiotic preparations intended for use in food-producing animals, other than topical and ophthalmic preparations, are not generally

recognized among qualified experts as having been shown to be safe for their intended use(s) within the meaning of section 201(s) of the Federal Food, Drug, and Cosmetic Act.

(e) Therefore, all exemptions from the provisions of section 409 of the act for use of antibiotics in food-producing animals based on sanctions or approvals granted prior to enactment of the Food Additives Amendment of 1958 (Pub. L. 85-929; 72 Stat. 1784) will be revoked and the uses which are concluded to be safe will be covered by food additive regulations. On those products for which there are inadequate residue data, actions will be initiated to amend or revoke antibiotic regulations under the provisions of section 507 of the act, or to withdraw approval of new-drug applications under the provisions of section 505 of the act. Antibiotic preparations, other than those for topical and ophthalmic application in food-producing animals, which are not covered by food additive regulations will be subject to regulatory action within 180 days after publication of the forthcoming revocation order.

(f) Because of the variation in the period of time that antibiotic residues may remain in edible products from treated animals, all injectable, intramammary infusion, intrauterine, and oral preparations (except certifiable antibiotics), including medicated premixes intended for use in food-producing animals, are deemed to be new drugs as well as food additives. An Antibiotic Form 6 (see § 431.50 of this chapter) will be required for all medicated premixes containing certifiable antibiotics.

(Sec. 409, 505, 507, 52 Stat. 1052, as amended, 59 Stat. 463, as amended, 72 Stat. 1785 et seq., as amended; 21 U.S.C. 355, 357)

§ 510.112 Antibiotics used in veterinary medicine and for nonmedical purposes; required data.

(a) An ad hoc committee, Committee on the Veterinary Medical and Non-medical Uses of Antibiotics, was formed by the Food and Drug Administration to study, and advise the Commissioner on, the use of antibiotics in veterinary medicine and for various nonmedical purposes as such uses may

affect the enforcement of the Federal Food, Drug, and Cosmetic Act with respect to the safety and effectiveness of such substances. A copy of the report may be obtained from the Food and Drug Administration, Office of Public Affairs, Room 15B-42, Parklawn Building, 5600 Fishers Lane, Rockville, MD 20857.

(b) On the basis of the report of the Committee and other information, sponsors of drugs containing any antibiotic intended for use in food-producing animals shall submit data for determining whether or not such antibiotics and their metabolites are present as residues in edible tissues, milk, and eggs from treated animals; however, in the case of a drug for which such data have already been submitted and for which a regulation has been promulgated under section 409 of the act, only such data as has been accumulated since the issuance of the regulation need be submitted.

(c) The required data shall be submitted within 180 days of the date of publication of this section in the FEDERAL REGISTER; except that in the case of data on intramammary infusion preparations the data shall be submitted within 60 days of such publication. Data demonstrating the absence in milk of residues of intramammary infusion preparations when used as directed in their labeling are needed within the 60-day period because of the importance of milk in the human diet.

(d) Regulatory proceedings including revocation of prior sanctions, or actions to suspend or amend new drug or antibiotic approvals granted prior to passage of the Food Additives Amendment of 1958 (72 Stat. 1784), may be initiated with regard to the continued marketing of any antibiotic preparation on which the required information is not submitted within the period of time prescribed by paragraph (c) of this section.

(e) Questions relating to the acceptability of proposed research protocols and assay methods for determining the amount of antibiotic residues in food should be directed to the Director, Bureau of Veterinary Medicine, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

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(Secs. 409, 505, 507, 52 Stat. 1052, as amended, 59 Stat. 463, as amended, 72 Stat. 1785; 21 U.S.C. 355, 357)

[40 FR 13807, Mar. 27, 1975, as amended at 46 FR 8460, Jan. 27, 1981]

§ 510.120 Suspension of approval of new-drug applications for certain diethylstilbestrol and diethylstilbestrol-containing drugs.

In the matter of suspension of approval of New-Drug Application Nos. 7175, 7310, 8254, 9105, 9506, 9532, 11121: (Mattox and Moore, Inc., Indianapolis, IN; Vineland Poultry Laboratories, Vineland, NJ; George N. Bell Co., Indianapolis, IN, respondents (FDC-D-49, 50, and 55)).

Following the public hearing held in the above-identified matter, beginning on April 25, 1960, and finally terminating on June 17, 1960, and issuance of tentative findings of fact, conclusions of law and facts, and tentative order, the Commissioner of Food and Drugs on December 15, 1961, issued final findings of fact, conclusions of law and facts and a final order. This final order concluded that all the products involved were unsafe within the meaning of section 505(e) of the Federal Food, Drug, and Cosmetic Act, in that the drug diethylstilbestrol is capable of producing and has produced cancer in animals and that this drug may be expected to produce, excite or stimulate the growth of certain cancers in human beings.

This final order was appealed to the U.S. District Court for the District of New Jersey, pursuant to the then effective provisions of section 505(h) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(h)). On August 20, 1964, this Court set aside this final order and remanded the case to the Food and Drug Administration with directions to reconsider the case in conformity with the opinion of the Court. (Goldhaft et al. v/a Vineland Poultry Laboratories v. George P. Larrick, et al.; Civil Action No. 122-62.)

Pursuant to the above-described opinion and order of the Court this case has been reconsidered.

Based on the substantial evidence of record, and pursuant to section 505(e) of the act (21 U.S.C. 355(e)) and Part 310 of Title 21 of the Code of Federal Regulations.

It is ordered, That:

1. New-Drug Application 7175, covering the drug "Tend-A-Wate," filed by Mattox & Moore, Inc., be, and is hereby suspended.

2. New-Drug Application 9532, covering the drugs "Tend-A-Wate 537," "Tend-A-Wate 539," and "Tend-A-Wate 545," filed by Mattox & Moore, Inc., be, and is hereby suspended.

3. New-Drug Application 7310, covering the drug "Tenderettes," filed by Vineland

Poultry Laboratories, be, and is hereby suspended.

4. New-Drug Application 9105, covering the drug "Caponade," filed by Vineland Poultry Laboratories, be, and is hereby suspended.

5. New-Drug Application 11121, covering the drug "Stilbosert," filed by George N. Bell, Manufacturing Chemists, be, and is hereby suspended.

6. New-Drug Application 8254, covering the drug "No-Brood," filed by Mattox and Moore, Inc., be, and is hereby suspended.

7. New-Drug Application 9506, covering the drug "Anti-Brood," filed by Vineland Poultry Laboratories, be, and is hereby suspended.

(Secs. 505(e), 52 Stat. 1053; 76 Stat. 782; (21 U.S.C. 355(e)))

Subpart C—Exportation of New Animal Drugs

§ 510.200 Export of new animal drug.

Before a new animal drug or an animal feed bearing or containing a new animal drug may be exported, it must comply with the regulations promulgated under section 512 of the act.

Subpart D—Records and Reports

§ 510.300 Records and reports concerning experience with new animal drugs for which an approved application is in effect.

(a) On receiving notification that an application submitted pursuant to § 514.1 of this chapter for a new animal drug is approved, the applicant shall establish and maintain such records and make such reports as are specified in this section to facilitate a determination as to whether there may be grounds for suspending or withdrawing approval of the application or whether any applicable regulation should be amended or repealed. The applicant shall maintain adequately organized and indexed files containing full reports of information pertinent to the safety or effectiveness of the new animal drug that have not previously been submitted as part of his application for the drug and which are received or otherwise obtained by him from any source, as follows:

(1) Unpublished reports of clinical or other animal experience, studies, in-

vestigations, and tests conducted by the applicant or reported to him by any person involving the new animal drug that is the subject of the application or any related drugs. An adequate summary and bibliography of reports in the scientific literature would ordinarily suffice. (The application must identify at the time of each report submission, each drug he considers related to the subject drug.)

(2) Experience, investigations, studies, or tests involving the chemical or physical properties or any other properties of the new animal drug, such as its behavior or properties in relation to microorganisms, including both the effects of the drug on microorganisms and the effect of microorganisms on the drug.

(3) For information required by this section, adequate identification of its source, when known, including the name and post office address of the person who furnishes such information.

(4) Copies of all mailing pieces and other labeling, and, if it is a prescription new animal drug, all advertising other than that contained in the application used in promoting the drug, and copies of the currently used package labeling that gives full information for use of the drug whether or not such labeling is contained in the application.

(5) Information concerning the quantity of the new animal drug distributed in a manner and form that facilitates estimates of the incidence of any adverse effects reported to be associated with the use of the drug. This does not require disclosure of financial, pricing, or sales data.

(6) Information concerning any previously unreported changes from the conditions described in an application conforming to the conditions of § 514.8(a)(5) of this chapter.

(b) The applicant shall submit to the Food and Drug Administration copies of the records and reports described in paragraph (a) of this section, except routine assay and control records, appropriately identified with the new animal drug application(s) to which they relate, as follows:

(1) Immediately upon receipt by the applicant, complete records or reports

covering information of the following kinds:

(i) Information concerning a mixup in the new animal drug or its labeling with another article.

(ii) Information concerning any bacteriological or significant physical or other change or deterioration in the new animal drug, or any failure of one or more distributed batches of the drug to meet the specifications established for it in the new animal drug application.

(2) As soon as possible, and in any event within 15 working days of its receipt by the applicant, complete records of reports concerning any information of the following kinds:

(i) Information concerning any unexpected side effects, injury, toxicity, or sensitivity reaction or any unexpected incidence or severity thereof associated with clinical use, studies, investigations, or tests, whether or not determined to be attributable to the new animal drug, except that this requirement shall not apply to the submission of information described in a written communication to the applicant from the Food and Drug Administration as types of information that may be submitted at other designated intervals. "Unexpected" as used in this subdivision refers to conditions or developments not previously submitted as part of the new animal drug application, or conditions and developments occurring at a rate higher than that shown by information previously submitted as part of the application.

(ii) Information concerning any unusual failure of the new animal drug to exhibit its expected pharmacological activities.

(3) When mailing pieces, any other labeling, and advertising are devised for promotion of the new animal drug, specimens shall be submitted at the time of initial dissemination of such labeling and at the time of initial publication of any advertisement for a prescription drug. Mailing pieces and labeling designed to contain samples of a drug shall be complete except for the omission of the drug.

(4) All the kinds of information described in paragraph (a) of this section, other than that submitted under the provisions of paragraphs (b) (1),

(2), and (3) of this section, shall be submitted as follows unless otherwise ordered in a written communication from the Commissioner:

(i) At intervals within 6 months beginning with the date of approval of the new animal drug application during the first year following such date, and at yearly intervals thereafter.

(ii) Whenever an applicant is required to submit reports under the provisions of paragraph (b)(4)(i) of this section with respect to more than one approved application for preparations containing the same new animal drug so that the same item(s) of information is (are) required to be reported for more than one application, he may elect to submit as a part of the report for one such application all the information common to such applications in lieu of reporting separately and repetitively on each. The applicant shall state when this is done and identify all the new animal drug applications for which the reports are submitted.

(iii) The submitted copies of records and reports shall include all the required information that was received or otherwise obtained by the applicant during the designated intervals.

(5) On written order of the Commissioner, within the time stated in such order or agreed to by the applicant and the Commissioner, any designated records or reports containing the kinds of information described in this section shall be submitted.

(c) The applicant shall, upon request of any properly authorized officer or employee of the Department at reasonable times, permit such officers to have access to and copy and verify any records and reports established and maintained under the provisions of this section.

(d) If the Food and Drug Administration finds that the applicant has failed to establish a system for maintaining required records or has repeatedly or deliberately failed to maintain such records or to make required reports in accordance with the provisions of this section, or that the applicant has refused to permit access to or copying of, or verification of such records or reports, the Commissioner shall give the applicant notice and op-

portunity for a hearing on the question of whether to withdraw the approval of the application, as provided in § 514.200 of this chapter.

(e) Upon written request of the applicant stating reasonable grounds therefor, the Commissioner will make available any information in possession of the Food and Drug Administration of the kinds the applicant is required to maintain under the provisions of this section, except information readily available to the applicant from other sources or information which the Commissioner concludes is confidential.

(f) The "applicant" required to establish and maintain records and make reports required by this section includes any person whose name appears on the labeling of the drug as its manufacturer, packer, or distributor under an approval or who is engaged in the manufacturing, processing, packing, or labeling of the drug under an approval of the new animal drug application or any supplement to it; however, to avoid unnecessary duplication in the submission of reports, any such applicant's obligation to submit a report may be met by its submission on his behalf, designated as such, by another person responsible for reporting.

§ 510.301 Records and reports concerning experience with animal feeds bearing or containing new animal drugs for which an approved application is in effect.

Records and reports of clinical and other experience with the new animal drug will be maintained and reported, appropriately identified with the new animal drug application(s) to which they relate, to the Bureau of Veterinary Medicine in duplicate in accordance with the following:

(a) Immediately upon receipt by the applicant, complete records or reports covering information of the following kinds:

(1) Information concerning any mixup in the new animal drug or its labeling with another article.

(2) Information concerning any bacteriological, or any significant chemical, physical, or other change or dete-

rioration in the drug, or any failure of one or more distributed batches of the drug to meet the specifications established for it in the new animal drug application.

(b) As soon as possible, and in any event within 15 working days of its receipt by the applicant, complete records or reports concerning any information of the following kinds:

(1) Information concerning any unexpected side effect, injury, toxicity, or sensitivity reaction or any unexpected incidence or severity thereof associated with clinical uses, studies, investigations, or tests, whether or not determined to be attributable to the new animal drug, except that this requirement shall not apply to the submission of information described in a written communication to the applicant from the Food and Drug Administration as types of information that may be submitted at other designated intervals. "Unexpected" as used in this paragraph refers to conditions or developments not previously submitted as part of the new animal drug application or not encountered during clinical trials of the drug, or conditions or developments occurring at a rate higher than shown by information previously submitted as part of the new animal drug application or at a rate higher than encountered during such clinical trials.

(2) Information concerning any unusual failure of the new animal drug to exhibit its expected pharmacological activity.

§ 510.302 Reporting forms.

(a) The information described in § 510.300, except that described in paragraphs (b) (1) and (2) of that section, shall be submitted appropriately identified with the new animal drug application(s) to which they relate in duplicate on Form FD-2301 "Transmittal of Periodic Reports and Promotional Material for New Animal Drugs."

(b) All adverse experiences with new animal drugs as described in § 510.300(b)(2) or § 510.301(b) whether or not related to a required periodic report submitted on a Form FD-2301, shall be reported on Form FD-1932 "Adverse Drug Reaction" (except as

provided in paragraph (c) of this section). Reports of adverse drug experiences may be submitted initially in the form of a written communication, but any such communication shall be followed promptly (but not necessarily within the prescribed 15 working days) by a completed Form FD-1932. A separate "Adverse Drug Reaction" form should be submitted for each patient where feasible.

(c) In lieu of Form FD-1932 the holder of an approved new animal drug application may submit:

(1) A computerized report if the information contained therein and the sequence in which it is presented are equivalent to that required by Form FD-1932 and the report is submitted in duplicate. Such reports will require initial approval by the Food and Drug Administration prior to use; and

(2) Copies of reports of reactions appearing in the published scientific literature may be submitted.

(d) Forms FD-1932 and FD-2301, with instructions for their use, may be obtained from the Food and Drug Administration, Department of Health and Human Services, Bureau of Veterinary Medicine, 5600 Fishers Lane, Rockville, MD 20857.

[40 FR 13807, Mar. 27, 1975, as amended at 41 FR 35844, Aug. 25, 1976]

§ 510.305 Maintenance of copies of approved applications for animal feed bearing or containing new animal drugs.

Each applicant shall maintain in a single accessible location on the premises of each establishment to which an approved medicated feed application (Form FDA 1900) or supplemental application applies either:

(a) A copy of the approved medicated feed application (Form FDA 1900) and a sample of the approved labeling; or

(b) Identification of the approved medicated feed application in a single file or in a single readable document that includes:

(1) The application number and date of its approval;

(2) The name(s) of the premix(es) and the concentration of the drug(s) contained in the premix(es);

- (3) The name(s) of the approved manufacturer(s) of the premix(es);
- (4) The concentration of the drug(s) in the finished medicated feed; and
- (5) A sample of the approved labeling.

[41 FR 36203, Aug. 27, 1976, as amended at 51 FR 7301, Mar. 3, 1986]

§ 510.310 Records and reports for new animal drugs approved before June 30, 1963.

(a) This section applies to new animal drugs, including antibiotics and medicated feed premixes bearing or containing new animal drugs, approved before June 30, 1963, on the basis of a new drug application, master file, antibiotic regulation, or food additive regulation.

(b) Sponsors of new animal drugs identified in paragraph (a) of this section shall submit the following information, in duplicate, for each dosage form of each such drug by November 21, 1980:

(1) If the new animal drug is currently marketed:

(i) A copy of the label on the package of the drug and of the package insert or brochure bearing directions or information for use of the product.

(ii) If the label, brochure, or package insert is not identical in content to the one for the new animal drug as originally approved, the sponsor shall also report what changes have been made (other than minor changes in arrangement or printing or changes of an editorial nature) and explain why they were made, and shall submit data supporting such changes if the data have not previously been submitted.

(iii) If clinical experience reported to or otherwise received by the sponsor indicates the need for change in claims for effectiveness or in side effects, warnings, or contraindications in the labeling or advertising currently in use, the sponsor shall submit a supplemental application proposing such changes in the labeling and a showing that any advertising will be appropriately revised.

(iv) If the clinical or other experience reported to or otherwise obtained by the sponsor has revealed any information concerning any side effect, injury, toxicity, or sensitivity reaction,

or any unexpected incidence or severity thereof, which by kind, or incidence or severity is not fully disclosed in the labeling, whether or not determined to be attributable to the drug, this information shall be submitted. Such information shall include full reports of all available information with respect to any deaths apparently related to a drug administration whether or not determined to be attributable to the drug. Any such information previously submitted need not be resubmitted.

(v) If the clinical or other experience reported to or otherwise obtained by the sponsor within the past 2 years has revealed any information with respect to a distributed batch concerning any mixup in the drug or its labeling with another article; any bacteriological or any significant chemical, physical, or other change or deterioration of the drug; or any failure of one or more distributed batches to meet specifications established in the new animal drug application or in the antibiotic regulations, this information shall be submitted. Any unresolved experience of the kinds listed in this paragraph shall be reported even though it occurred before the 2-year period.

(2) If the new animal drug is no longer marketed, but it is the subject of an approval that is still in effect:

(i) Identification of the dosage form of the new animal drug or medicated feed premix by its established and proprietary names, if any;

(ii) The formula showing quantitatively each ingredient of the drug to the extent disclosed on the label (a copy of the label will ordinarily fulfill this requirement);

(iii) The route of administration;

(iv) The new animal drug or other identification or application number;

(v) The date and reason for discontinuing its marketing.

(c) Approval of applications covering products which are no longer marketed may be withdrawn under § 514.115 of this chapter on the basis of a request for its withdrawal submitted in writing by a person holding an approved application. Such withdrawal of approval will be made on the ground that the drug subject to such application is no longer being market-

ed, provided information is furnished in support of this finding and provided certain other conditions exist as specified in that section. A written request for such withdrawal will be construed as a waiver of an opportunity for a hearing.

(d) Sponsors of new animal drugs identified in paragraph (a) of this section are exempt from the reporting requirements of this section if:

(1) Their product is no longer marketed, and information has previously been submitted to the Food and Drug Administration regarding discontinuation of marketing including the date and reason for such action, and any existing approval for the product has been withdrawn; or

(2) As a result of a supplemental approval granted beginning June 20, 1963, the sponsor is presently reporting under the requirements of § 510.300.

(e) After the submission of the initial reports required by paragraph (b) of this section, each sponsor shall maintain records and submit yearly reports of the kinds required by § 510.300.

(f) All reports required by this section shall be addressed to the Division of Surveillance (HFV-210), Bureau of Veterinary Medicine, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, and shall be distinctly marked "New Animal Drug (or Antibiotic) Report" together with the applicable new animal drug application number, antibiotic account number, or other identification on the envelope.

[45 FR 42261, June 24, 1980]

§ 510.350 Records of distribution of animal drugs subject to section 512(n) of the act.

(a) The person who requested certification shall keep complete records showing each shipment and other delivery (including exports) of each certified batch or part thereof by such person or by any person subject to his control. Such records shall show the date and quantity of each such shipment or delivery and the name and post-office address of the person to whom such shipment or delivery was

made, and shall be kept for not less than 3 years after such date.

(b) Upon the request of any other officer or employee of the Food and Drug Administration, or of any other officer or employee of the United States acting on behalf of the Secretary, the person to whom a certificate is issued shall at all reasonable hours make such records available to any such officer or employee and shall accord to him full opportunity to make inventory of stocks of such batch on hand and otherwise to check the correctness of such records.

Subpart E—Requirements for Specific New Animal Drugs

§ 510.410 Corticosteroids for oral, injectable, and ophthalmic use in animals; warnings and labeling requirements.

(a) The Food and Drug Administration has received reports of side effects associated with the oral, injectable, and ophthalmic use of corticosteroid animal drugs. The use of these drugs administered orally or by injection has resulted in premature parturition when administered during the last trimester of pregnancy. Premature parturition may be followed by dystocia, fetal death, retained placenta, and metritis. Additionally, corticosteroids used in dogs, rabbits, and rodents during pregnancy have produced cleft palate in offspring. Use in dogs has resulted in other congenital anomalies, including deformed forelegs, phocomelia, and anasarca. Drugs subject to this section are required to carry the veterinary prescription legend and are subject to the labeling requirements of § 201.105 of this chapter.

(b) In view of these potentially serious side effects, the Food and Drug Administration has concluded that the labeling on or within packaged corticosteroid-containing preparations intended for animal use shall bear conspicuously the following warning statement:

Warning: Clinical and experimental data have demonstrated that corticosteroids administered orally or by injection to animals may induce the first stage of parturition if used during the last trimester of pregnancy

and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis.

Additionally, corticosteroids administered to dogs, rabbits, and rodents during pregnancy have resulted in cleft palate in offspring. Corticosteroids administered to dogs during pregnancy have also resulted in other congenital anomalies, including deformed forelegs, phocomelia, and anasarca.

[49 FR 48535, Dec. 13, 1984]

§ 510.413 Chloroform used as an ingredient (active or inactive) in animal drug products.

(a) Chloroform has been used as an ingredient in animal drug products such as cough preparations, linaments, and some pastes. Although considered safe for many years, recent information has become available associating chloroform with carcinogenic effects in animals. Studies conducted by the National Cancer Institute have demonstrated that the oral administration of chloroform to mice and rats induced hepatocellular carcinomas (liver cancer) in mice and renal tumors in male rats.

(b) Any drug product intended for use in or on animals and containing chloroform as an ingredient is deemed to be either (1) a new animal drug within the meaning of section 201(w) of the act, and unsafe within the meaning of section 512 of the act and adulterated under section 501 of the act and subject to regulatory action under sections 301, 501, and 512 of the act; or (2) misbranded under section 502 of the act, and therefore subject to regulatory action under sections 301 and 502 of the act. Any animal drug product containing chloroform in residual amounts from its use as a processing solvent during manufacture of the drug product, or from the synthesis of a drug ingredient, is not, for the purpose of this regulation, considered to contain chloroform as an ingredient.

(c) Any holder of an approved new animal drug application for a drug product containing chloroform as an ingredient shall submit to the Food and Drug Administration on or before October 3, 1977, a supplemental application providing for a revised formulation removing chloroform as an ingredient.

(1) The supplemental application shall contain:

(i) A full list of articles used as components and a full statement of the composition of the drug product.

(ii) The date that the composition of the drug product will be changed.

(iii) Data showing that the change in composition does not interfere with any assay or other control procedures used in manufacturing the drug product, or that the assay and other control procedures are revised to make them adequate.

(iv) Data available to establish the stability of the revised formulation and, if the data are too limited to support a conclusion that the drug will retain its declared potency for a reasonable marketing period, a commitment from the applicant:

(a) To test the stability of marketed batches at reasonable intervals;

(b) To submit the data as they become available; and

(c) To recall from the market any batch found to fall outside the approved specifications for the drug.

(v) Copies of the label and all other labeling to be used for the drug product—a total of nine copies if in final printed form, three copies if in draft form.

(2) If such drug product contains more than 1 percent chloroform, the revised formulation containing no chloroform shall not be marketed before the receipt of written notice of approval of the supplemental application by the Food and Drug Administration.

(3) If such drug product now contains 1 percent or less chloroform, the revised formulation containing no chloroform may be marketed after submission of the supplemental application but prior to the receipt of written notice of its approval by the Food and Drug Administration.

(d) Any sponsor of a "Notice of Claimed Investigational Exemption for a New Animal Drug" (INAD notice) for an animal drug product containing chloroform as an ingredient shall amend the INAD notice on or before October 3, 1977, to revise the formulation removing chloroform as an ingredient.

(e) The Commissioner will initiate action to withdraw approval of a new animal drug application or terminate an INAD notice in accordance with the applicable provisions of section 512 of the act and Parts 511 and 514 of this chapter upon failure of a holder of an approved new animal drug application or sponsor of an INAD notice to comply with the provisions of paragraph (c) or (d) of this section.

(f) Any drug product intended for animal use containing chloroform as an ingredient that is introduced or delivered for introduction into interstate commerce following the effective date of this regulation will be subject to regulatory action under sections 301, 501, 502, and 512 of the act.

(Secs. 301, 501, 502, 512, 701(a), 52 Stat. 1042-1043 as amended, 1049-1050 as amended, 1055, 52 Stat. 343-351 (21 U.S.C. 331, 351, 352, 360b, 371(a)))

(42 FR 44226, Sept. 2, 1977)

§ 510.440 Injectable iron preparations.

There has been an increasing interest in the use of injectable iron compounds for the prevention or treatment of iron-deficiency anemia in animals. Although some such preparations have been shown to be safe, such articles are regarded as new animal drugs within the meaning of the Federal Food, Drug, and Cosmetic Act. Accordingly, an approved new animal drug application is required prior to the marketing of such preparations within the jurisdiction of the act. In addition to the need for demonstrating the safety of such articles, the labeling of such preparations should not only recommend appropriate dosages of iron but also declare the amount (in milligrams) of available iron (Fe) per milliliter of the subject product.

§ 510.450 Sulfonamide-containing drugs for oral, injectable, intramammary, or intrauterine use in food-producing animals.

(a) The Commissioner of Food and Drugs announced in the FEDERAL REGISTER of October 23, 1970 (35 FR 16538) the need for additional information regarding the labeling and residues of sulfonamide-containing drugs as follows:

(1) New information available to the Commissioner of Food and Drugs has shown that, under certain circumstances where food-producing animals have been treated with oral or parenteral sulfonamide-containing drugs, sulfonamide residues may be detected in the edible products of such animals when they are slaughtered within 10 days of the last treatment.

(2) The presence of sulfonamide residues in food constitutes an adulteration within the meaning of section 402(a)(2)(D) of the act in the absence of a tolerance for such residues established pursuant to section 512(i) of the act.

(3) To assure that edible products from treated animals are safe for human consumption, the labeling of preparations which contain sulfonamide drugs intended for oral or parenteral use and which are not the subject of a regulation providing for such use shall bear:

(i) A statement that the use of the drug must be discontinued 10 days before treated animals are slaughtered for food; or

(ii) A statement of withdrawal period which has been established based upon data submitted to the Commissioner and found satisfactory for the elimination of drug residues from edible products.

(4) Labeling revisions required for compliance with this paragraph were made at the earliest possible time and, in any case by January 21, 1971. Any such products now on the market and not in compliance with this paragraph are subject to regulatory action.

(5) The labeling requirements of paragraph (a)(3)(i) of this section were adopted as an interim measure. Sponsors of sulfonamide-containing drugs subject to the provisions of this section were required to submit by October 22, 1971, adequate data to permit the establishment of appropriate withdrawal periods as required by paragraph (a)(3)(ii) of this section.

(b) Recently available studies indicate that the degree of thyroid response to exposure to sulfonamide drugs should be given greater significance in the evaluation of sulfonamide toxicity and in the determination of "no-effect" levels of the drugs in labo-

ratory animals to support the establishment of tolerances for negligible residues of sulfonamides, in edible products from treated animals.

(c) The Commissioner has concluded that because of questions raised regarding sulfonamide toxicity there is a need to facilitate a determination of whether there are grounds to invoke section 512(e) of the act regarding the continued use of these sulfonamide-containing drugs. Therefore, it has been concluded that sulfonamide-containing drugs for oral, injectable, intrauterine or intramammary use in food-producing animals are new animal drugs for which approved new animal drug applications are required. All persons or firms marketing such drugs which are not now the subject of an approved new animal drug application must submit a complete new animal drug application on or before January 20, 1975 for these drugs if marketing is to continue during the interim. Any such drug then on the market which is not the subject of an application submitted for such drug will be deemed adulterated within the meaning of section 501(a)(5) of the act and subject to regulatory action. The submission of applications for sulfonamide-containing drugs pursuant to § 558.15 (38 FR 9811) which were required to be submitted by July 19, 1973 will be adequate to meet the requirements for submission of an application pursuant to this section.

(d) Under the provisions of section 512(1) of the act, by October 22, 1975, each sponsor of a new animal drug application for a sulfonamide-containing drug labeled for oral, injectable, intrauterine or intramammary use in food-producing animals shall submit, for each such drug, the results of 90-days subacute toxicity studies in one rodent and one non-rodent species. The studies shall include a determination of a "no-effect" level of the drug using thyroid response as one parameter. Protocols may be submitted to the Food and Drug Administration for review prior to the initiation of studies. If an evaluation of the results of these studies shows that existing methodology used to establish negligible tolerances for residues of the sulfonamide drugs in edible tissues is not of adequate sensi-

tivity and specificity, improved methodology will be required. Any such drug then on the market which is not the subject of such submitted studies will be subject to the provisions of section 512(e)(2)(A) of the act.

(e) To assure that edible products from treated swine are safe for human consumption, the labeling of preparations which contain sulfamethazine intended for use in swine feed or drinking water shall, in lieu of the labeling requirement set forth in paragraph (a) of this section, bear a statement that the use of the drug must be discontinued 15 days before treated animals are slaughtered for food.

(f) New animal drug applications and the data required by this section pursuant to section 512(1) of the act shall be submitted to the Food and Drug Administration, Bureau of Veterinary Medicine, Division of New Animal Drugs, HFV-300, 5600 Fishers Lane, Rockville, MD 20857.

[40 FR 13807, Mar. 27, 1975, as amended at 40 FR 43213, Sept. 19, 1975; 43 FR 19385, May 5, 1978; 48 FR 3964, Jan. 28, 1983]

§ 510.455 New animal drug requirements regarding free-choice administration in feeds.

(a) For the purpose of this section, free-choice administration of animal drugs in feeds involves feeds that are placed in feeding or grazing areas and are not intended to be consumed fully at a single feeding or to constitute the entire diet of the animal. Such methods of administering drugs include, but are not limited to, medicated blocks (agglomerated feed compressed or rendered into a solid mass and cohesive enough to hold its form), mineral mixes, and liquid feed tank supplements ("lick tank" supplements) containing one or more animal drugs. The manufacture of medicated free-choice feeds is subject to the current good manufacturing practice regulations for medicated feeds.

(b) The Food and Drug Administration has concluded that there are questions about the safety and effectiveness of drugs when administered in free-choice feeds. Therefore, such methods of administration cause the drugs so administered to be new

animal drugs, for which approved new animal drug applications (NADA's) are required. (See § 510.3(i)). In addition, the exemption from the requirement of an approved medicated feed application provided in § 558.4 of this chapter does not apply to any free-choice medicated feed.

(c) An NADA or supplemental NADA for products for free-choice feeding submitted for approval under section 512(b) of the act shall provide for:

(1) The manufacture of a finished product for the free-choice administration of a new animal drug. Such an approval will not provide a basis upon which an application can be approved under section 512(m) of the act; or

(2) The manufacture of a Type A medicated article for use in the subsequent manufacture of a free-choice medicated feed. The approved NADA will provide a basis upon which an application can be approved under section 512(m) of the act. Data for a specific free-choice product may, if desired, be generated and submitted to the Food and Drug Administration by the manufacturer of the free-choice feed in the form of a master file which can be referenced in the NADA or supplemental NADA submitted by the new animal drug sponsor.

(d) Approval of the NADA or supplemental NADA submitted under paragraph (c) of this section will be reflected in a regulation in Part 558 of this chapter published under section 512(i) of the act. The regulation will either state the formulation of the approved free-choice product or specify the specific free-choice administration products in which the drug is approved for use. If the approval is for a Type A medicated article, the regulation in Part 558 of this chapter will indicate that each use of the Type A medicated article in a free-choice product must be the subject of an approved supplemental NADA.

(e) An application submitted under section 512(m) of the act to provide for manufacture of a specific free-choice feed from an approved Type A medicated article will be approved if, in addition to the information required by the medicated feed application, it includes a reference to the

exact formula of the product to be manufactured as follows:

(1) The formula is the same as the one published in the new animal drug regulations; or

(2) The data in a master file have been referenced in an NADA or supplemental NADA; and

(3) Use of the Type A medicated article in the specific formulation has been approved on the basis that:

(i) The formula is the same as the one for which acceptable data have been submitted in a master file by the medicated feed applicant; or

(ii) The medicated feed applicant has written authority to reference a master file that has acceptable data for the formula in question.

(Information collection requirements were approved by the Office of Management and Budget under control number 0910-0205)

[51 FR 19827, June 3, 1986]

Subpart F—Animal Use Exemptions From Certification and Labeling Requirements

AUTHORITY: Sec. 507, 59 Stat. 463 as amended (21 U.S.C. 357).

§ 510.510 Antibiotic drugs for use in medicated animal feed (antibiotic medicated feed premixes).

Antibiotic drug premixes subject to section 512(n) of the act shall be exempt from the certification requirements under the conditions specified in § 510.5(b).

§ 510.515 Animal feeds bearing or containing new animal drugs subject to the provisions of section 512(n) of the act.

Animal feeds that bear or contain penicillin, streptomycin in combination with penicillin, chlortetracycline, feed grade zinc bacitracin, and bacitracin methylene disalicylate, with or without added suitable nutritive ingredients are exempt from the certification requirements of section 512 of the act provided they are the subject of and in compliance with regulations for their use in this Subchapter E, Part 558 of this chapter, or any one of the paragraphs of this section:

(a) Where indicated in paragraph (b) of this section it is manufactured with

or without one, but only one, of the following ingredients in a quantity, by weight of feed, as hereinafter indicated:

(1) Arsanilic acid: Not less than 0.005 percent and not more than 0.01 percent.

(2) Sodium arsanilate: Not less than 0.005 percent and not more than 0.01 percent.

(3) 3-Nitro-4-hydroxyphenylarsonic acid: Not less than 0.0025 percent and not more than 0.0075 percent except in chicken or turkey feed which shall contain not less than 0.0025 percent and not more than 0.005 percent.

(4) Furazolidone: 0.00083 percent.

(5) Furazolidone 0.00083 percent, with or without nitrofurazone 0.0056 percent, and/or 3-nitro-4-hydroxyphenylarsonic acid not less than 0.0025 percent and not more than 0.0075 percent except in chicken or turkey feed in which the limit of 3-nitro-4-hydroxyphenylarsonic acid shall be not less than 0.0025 percent and not more than 0.005 percent.

(b) It is intended for use in any one of the following conditions set forth in this paragraph:

(1)–(6) [Reserved]

(7)(i) It is intended for use solely as a treatment for complicated, chronic respiratory disease (air-sac infection), infectious sinusitis, blue comb (nonspecific infectious enteritis, mud fever), and hexamitiasis in poultry, and/or bacterial swine enteritis; its labeling contains adequate directions and warnings for such use; and it contains, per ton of feed, not less than 100 grams of chlortetracycline, or oxytetracycline, or a combination of such drugs, or not less than 90 grams nor more than 180 grams of penicillin and streptomycin in a combination containing 16.7 percent penicillin.

(a) When intended for the uses specified in this paragraph (b)(7)(i), it may also contain, in the amount specified, one, but only one, of the ingredients prescribed by paragraph (a) of this section. If it is intended for use solely in poultry, it may contain 0.1 percent of para-aminobenzoic acid or the sodium or potassium salt of para-aminobenzoic acid.

(b) If it is intended for use solely in the treatment of the diseases of chick-

ens described in this paragraph (b)(7)(i), it contains, per ton of feed, not less than 100 grams and not more than 260 grams of chlortetracycline and it contains not less than 0.4 percent and not more than 0.8 percent of dietary calcium, then representations may be made in its labeling to the effect that the reduced amount of calcium aids in increasing the concentrations of the antibiotic in the blood of treated birds; the labeling of such medicated feed shall include that required by § 558.128 of this chapter.

(c) If it is intended for use solely as a treatment for bacterial swine enteritis, it may contain, per ton of feed, not less than 90 grams nor more than 270 grams of penicillin and streptomycin in a combination containing 16.7 percent penicillin, provided that its labeling bears a warning that the feed is not to be used for more than 14 days.

(ii) [Reserved]

(iii) It is also intended for use in the treatment of coccidiosis in chickens caused by *E. tenella* and *E. necatrix*; its labeling bears adequate directions and warnings for such use (including the directions and warnings required by paragraph (b)(7)(i) of this section); and it contains, per ton of feed, 200 grams of chlortetracycline and 0.4 percent to 0.55 percent of dietary calcium.

(8)–(9) [Reserved]

(10) It is intended for use solely in the treatment of chronic respiratory disease (air-sac infection), infectious sinusitis, and blue comb (nonspecific infectious enteritis) in poultry and/or bacterial swine enteritis; its labeling bears adequate directions and warnings for such use; and it contains, per ton of feed, the equivalent of 100 grams of penicillin. When intended for uses specified in this paragraph, it may also contain, in the amount specified, one, but only one, of the ingredients prescribed by paragraph (a) of this section.

(11) It is intended for use solely as a treatment for bacterial swine enteritis caused by *Salmonella choleraesuis*, its labeling bears adequate directions and warnings for such use, and it contains nitrofurazone in a quantity, by weight of feed, of 0.056 percent.

(12) [Reserved]

(13) It is intended for use solely in the treatment of chronic respiratory disease (air-sac infection) and infectious sinusitis in poultry; its labeling bears adequate directions and warnings for such use; and it contains not less than 0.1 percent para-aminobenzoic acid or the sodium or potassium salt or para-aminobenzoic acid.

(14) [Reserved]

(15) It is intended for use solely as an aid in the treatment of poultry in outbreaks of fowl typhoid, pullorum, the paratyphoids, infectious arthritis due to a filterable agent, histomoniasis (blackhead), hexamitiasis, quail disease (ulcerated enteritis), paracolon infection, avian infectious hepatitis, and coccidiosis, its labeling bears adequate directions and warnings for such use; and it contains the following quantities of furazolidone, by weight of feed, for the conditions indicated:

(i) For fowl typhoid, pullorum, and the paratyphoids in birds regardless of age: 0.011 percent.

(ii) For the treatment of histomoniasis (blackhead), paracolon infection, and avian infectious hepatitis of chickens, and to lessen the morbidity in outbreaks of infectious arthritis due to a filterable agent: 0.022 percent.

(16) [Reserved]

(17)(i) It is intended for use solely as an aid in the treatment of chronic res-

piratory disease (air-sac infection), infectious sinusitis, blue comb (nonspecific infectious enteritis, mud fever) in poultry; its labeling bears adequate directions and warnings for such use; and it contains not less than 100 grams of chlortetracycline or oxytetracycline or a combination of these two drugs per ton of food.

(ii) It is also intended for the treatment of the diseases of poultry specified in paragraph (b)(15) of this section; it contains one of the ingredients in the amount and under the conditions set forth in paragraph (b)(17)(i) of this section; and it contains furazolidone in the amount specified in paragraph (b)(15) of this section.

(18)—(24) [Reserved]

(25) It is a medicated cattle feed containing chlortetracycline in the amounts and for the purposes indicated in § 558.128 of this chapter, and its labeling bears adequate directions and warnings for such use.

(26)—(28) [Reserved]

(29) It is intended for use solely as an aid in reducing the incidence of bacterial diarrhea in laboratory mice; its labeling bears adequate directions and warnings for such use; and it contains not less than 100 grams of chlortetracycline per ton of feed.

(c) It is intended for use as follows:

Product	Species	Use levels	Indications for use
1. Nicarbazin.....	Chickens.....	0.01 to 0.02 percent.....	For use in the prevention of outbreaks of coccidiosis in poultry flocks; growth promotion and feed efficiency.
Procaine penicillin.....	do.....	2.4 to 50 g/ton.....	
2. Nicarbazin.....	do.....	0.01 to 0.02 percent.....	Do.
Bacitracin methylene disalicylate.....	do.....	4 to 50 g/ton.....	
3. Nicarbazin.....	do.....	0.01 to 0.02 percent.....	For use as an aid in the prevention of coccidiosis in poultry flocks; growth promotion and feed efficiency; improving pigmentation.
Bacitracin methylene disalicylate.....	do.....	4 to 50 g/ton.....	
3-Nitro-4-hydroxyphenylarsonic acid.....	do.....	0.0025 to 0.005 percent.....	Do.
4. Nicarbazin.....	do.....	0.01 to 0.02 percent.....	
Procaine penicillin.....	do.....	2.4 to 50 g/ton.....	
3-Nitro-4-hydroxyphenylarsonic acid.....	do.....	0.0025 to 0.005 percent.....	
5. Procaine penicillin.....	Swine.....	1.5 to 7.5 g/ton.....	Increase rate of gain and improve feed efficiency in growing swine; aid in the prevention of bacterial swine enteritis.
Streptomycin.....	do.....	7.5 to 37.5 g/ton.....	
Arsanilic acid.....	do.....	45 to 90 g/ton.....	

Product	Species	Use levels	Indications for use
6. Penicillin	Chickens and turkeys	2.4 to 25 g/ton	For use as a treatment for complicated chronic respiratory disease (air-sac infection), infectious sinusitis, blue comb (nonspecific infectious enteritis, mud fever), and hexamitiasis in poultry; as an aid in maintaining or increasing egg production of chickens, hatchability of eggs, prevention of early mortality of chicks when due to organisms that are sensitive to streptomycin and penicillin; and for increased weight gain and improving feed efficiency.
Streptomycin	do	15 to 75 g/ton	
7. Penicillin	Swine	5 to 25 g/ton	For use in the prevention and treatment of bacterial swine enteritis; for increased weight gain and improved feed efficiency.
Streptomycin	do	15 to 75 g/ton	
8. Furazolidone and— Bacitracin methylene disalcylate or— Zinc bacitracin or Procaine penicillin	Chickens and turkeys	0.011 percent	Growth promotion and feed efficiency. For prevention of fowl typhoid, paratyphoid, and pullorum in chickens and turkeys when fed for the first 2 weeks of the birds' life. For treatment of fowl typhoid, paratyphoid, and pullorum in chickens and turkeys when fed for at least 2 weeks, except when paratyphoid is due to <i>S. typhimurium</i> . For reduction of condemnations due to chronic respiratory disease air-sac complex associated with vaccination stress, feed continuously beginning at least 1 week before vaccination. For prevention of infectious hepatitis when fed continuously during the danger period. For control of coccidiosis in chickens, caused by <i>E. tenella</i> , <i>E. necatrix</i> , or <i>E. acervulina</i> when fed for 5 to 7 days or longer. For prevention of blackhead (histomoniasis, enterohepatitis) in chickens and turkeys when fed continuously. For prevention of paracolon in chickens and turkeys and hexamitiasis in turkeys when fed throughout the danger period. For control of chronic respiratory disease (air-sac), infectious sinusitis, synovitis (arthritis due to filterable agent), nonspecific enteritis (blue comb, mud fever) and quail disease (ulcerative enteritis) when fed for 5 to 10 days. (NOTE.—Severe outbreaks may require twice the level specified; i.e., 0.022 percent.)
	do	4-50 g/ton	
	do	2.4 to 50 g/ton	
9. Furazolidone and— Bacitracin methylene disalcylate or— Zinc bacitracin or Procaine penicillin	Chickens and turkeys	0.011 to 0.022 percent	Growth promotion and feed efficiency. Aid in maintenance of feed consumption and growth and reduction of mortality and morbidity due to stress; for the control of the following nonspecific conditions: chronic respiratory disease (air-sac), infectious sinusitis, synovitis (arthritis due to a filterable agent), nonspecific enteritis (blue comb, mud fever) and quail disease (ulcerative enteritis) when fed 5 to 10 days. Follow with preventive level to prevent recurrence.
	do	4 to 50 g/ton	
	do	2.4-50 g/ton	

Product	Species	Use levels	Indications for use
10. Furazolidone and— Bacitracin methylene disicylate or— Zinc bacitracin or Procaine penicillin	Chicken and turkeys. do. do.	0.22 percent 4 to 50 g/ton 2.4 to 50 g/ton	For treatment of paratyphoid due to <i>S. typhimurium</i> when fed for 2 weeks. For treatment of blackhead (histomoniasis, enterohepatitis) in chickens and turkeys when fed for 2 to 3 weeks (following diagnosis). For treatment of paracolon in chickens and turkeys and hexamitiasis in turkeys when fed for 2 weeks or longer (following diagnosis). For control of chronic respiratory disease (air-sac), infectious sinusitis, synovitis (arthritis due to filterable agent), mud fever and quail disease (ulcerative enteritis) when fed for 5 to 10 days. For treatment of infectious hepatitis in chickens when fed for 14 days and repeated as necessary.
11. Chlortetracycline	Swine	10 to 50 g/ton	Enhancement of growth and feed efficiency.
Arasnic acid	do	0.005 to 0.01 percent	
12. Chlortetracycline	Sheep	20 g/ton	As an aid in the reduction of losses due to enterotoxemia.
13. Chlortetracycline	do	80 mg per head per day	It is intended for use as an aid in reducing the incidence of vibronic abortion in breeding sheep; it is to be administered continuously during pregnancy.
14. Chlortetracycline	Cattle	Feed contains the following quantities of chlortetracycline, by weight, for the conditions indicated: (1) For the prevention of foot rot and as an aid in the reduction of bacterial diarrhea in dairy cattle; 0.1 mg/lb of body weight per day; and (2) as an aid in the reduction of losses due to respiratory infection (infectious rhinotracheitis—shipping fever complex) in dairy cattle: 0.1 mg/lb of body weight per day, except that if it is intended for use for more than 30 days it may contain chlortetracycline, in a quantity by weight of feed to provide 70 mg per head per day.	As an aid in the reduction of bacterial diarrhea in dairy cattle or as an aid in reduction of losses due to respiratory infection (infectious rhinotracheitis—shipping fever complex) or as an aid in the prevention of foot rot in cattle.

(Secs. 512, 701(a), 52 Stat. 1055, 82 Stat. 343-351 (21 U.S.C. 360b, 371(a); 21 CFR 5.1)

[41 FR 8299, Feb. 25, 1976, as amended at 41 FR 11011, Mar. 15, 1976; 42 FR 18614, Apr. 8, 1977; 47 FR 42102, Sept. 24, 1982; 47 FR 51563, Nov. 16, 1982]

§ 510.520 Exemption from batch certification requirements for antibiotic drugs for animal use subject to section 512(n) of the act.

(a) In addition to the exemptions from certification provided in §§ 510.510 and 510.515, antibiotic drugs subject to section 512(n) of the act are also exempt from the batch certification requirements under §§ 514.50 and 514.51 of this chapter, if the following conditions are met:

(1) The antibiotic drug is the subject of a new animal drug application approved under § 514.105 of this chapter.

(2) The antibiotic drug is packaged and labeled in accordance with the

conditions of marketing described in the approved new animal drug application.

(3) The bulk antibiotic drug used in preparing the antibiotic drug product meets the standards of identity, strength, quality, and purity specified in the applicable regulation (monograph) in this chapter.

(4) The antibiotic drug product meets the standards of identity, strength, quality, and purity specified in the applicable regulation (monograph) in this chapter.

(b) Nothing in this section prevents a manufacturer from applying for batch certification of an antibiotic

drug for animal use subject to an exemption under this section as provided in section 512(n)(3) of the act.

(c) All exemptions from batch certification requirements for antibiotic drugs for animal use under this section are subject to the conditions of effectiveness under § 510.521.

(d) Reporting/recordkeeping requirements contained in this Part 510 have been approved by the Office of Management and Budget and assigned approval numbers 0910-0007, 0910-0009, and 0910-0032.

(Secs. 505, 507, 512(n), 701(f) and (g), 52 Stat. 1050-1053 as amended, 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 355, 357, 360b(n), 371(f) and (g)))

[47 FR 39159, Sept. 7, 1982, as amended at 51 FR 30211, Aug. 25, 1986]

§ 510.521 Conditions on the effectiveness of exemptions of antibiotic drugs for animal use from batch certification requirements.

(a) If at any time after an exemption from batch certification requirements for an antibiotic drug for animal use has been granted, the Commissioner finds on the basis of new information before the agency with respect to such exempted drug, evaluated together with the evidence available to the agency when such exemption was granted, that certification of each batch is necessary to ensure its safety and efficacy of use, the Commissioner shall act immediately to revoke all exemptions from batch certification requirements granted for such drug.

(b) If the Commissioner finds that the person granted an exemption from batch certification requirements for an antibiotic drug for animal use subject to section 512(n) of the act has failed to comply with the requirements of section 512 of the act and the regulations promulgated thereunder; or if the Commissioner finds that the requirements of § 510.520 have not been met; or if the Commissioner finds that the petition for exemption from batch certification contains any false statements of fact, the Commissioner may revoke the exemption from batch certification requirements immediately and require batch certification of the drug until such person shows ade-

quate cause why the exemption from batch certification requirements should be reinstated.

(c) If the Commissioner repeals or suspends an exemption from batch certification requirements for an antibiotic drug for animal use, a notice to that effect and the reasons therefor will be published in the **FEDERAL REGISTER**.

(d) Any person who contests the revocation or suspension or denial of reinstatement of an exemption from batch certification requirements for an antibiotic drug for animal use shall have an opportunity for a regulatory hearing before the Food and Drug Administration under Part 16 of this chapter.

(Secs. 505, 507, 512(n), 701(f) and (g), 52 Stat. 1050-1053 as amended, 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 355, 357, 360b(n), 371(f) and (g)))

[47 FR 39159, Sept. 7, 1982]

Subpart G—Sponsors of Approved Applications

§ 510.600 Names, addresses, and drug labeler codes of sponsors of approved applications.

(a) Section 512(i) of the act requires publication of names and addresses of sponsors of approved applications for new animal drugs.

(b) In this section each name and address is identified by a numerical drug labeler code. The labeler codes identify the sponsors of the new animal drug applications associated with the regulations published pursuant to section 512(i) of the act. The codes appear in the appropriate regulations and serve as a reference to the names and addresses listed in this section. The drug labeler code is established pursuant to section 510 of the act.

(c) The names, addresses, and drug labeler codes of sponsors of approved new animal drug applications are as follows:

(1) ALPHABETICAL LISTING OF SPONSORS

Firm name and address	Drug labeler code
Abbott Laboratories, North Chicago, IL 60064	043731
Affiliated Laboratories Division, Whitmoyer Laboratories, Inc., 19 North Railroad St., Myerstown, PA 17067	011825
Ag-Mark, Inc., P.O. Box 127, Teechey, NC 28464	024174
Agri-Basics, ConAgra-Westfields, 1420 Minnesota Ave., Billings, MT 59101	023966
Agribusiness Marketers, Inc., 2967 West Dual, Baton Rouge, LA 70815	015563
Agri-Tech, Inc., 4722 Broadway, Kansas City, MO 64112	017762
Carl S. Akey, Inc., P.O. Box 607, Lewisburg, Ohio 45338	017790
A. L. Laboratories, Inc., A Subsidiary of A/S Apothekernes Laboratorium for Specialpræparater, One Executive Drive, P.O. Box 1399, Fort Lee, NJ 07024	046573
Albers Milling Co., Carnation Bldg., 5045 Wilshire Blvd., Los Angeles, CA 90036	017826
Albion Laboratories, Inc., 101 North Main, Clearfield, UT 84015	011485
Allied Pharmaceutical Division of K.C. Pharmaceutical, Inc., 1234 Clay St., North Kansas City, MO 64116	012963
Alena Inc., 60 Baylis Rd., Melville, NY 11747	025463
American Cyanamid Co., Berdan Ave., Wayne, NJ 07470	010042
American Scientific Laboratories, A Division of Schering Corp., Bloomfield, NJ 07003	000138
Anaquest, a Division of BOC, Inc., 100 Mountain Ave., Murray Hill, NJ 07974	010019
Anthony Products Co., 5600 Peck Rd., Arcadia, CA 91006	000864
Argent Laboratories, 8702 152d Ave. NE, Redmond, WA 98052	051212
Arkansas Micro Specialties Inc., P.O. Box 308, Highway 71 North, Lowell, AR 72745	047863
Ayerst Laboratories, Division of American Home Products Corp., 685 Third Ave., New York, NY 10017	000146
Babineux's Veterinary Products, Inc., 6425 Airline Highway, Metairie, LA 70003	021188
Balfour Guthrie & Co., Ltd., 315 North H St., Fresno, CA 93701	043728
Beechem Laboratories, Division of Beechan, Inc., Bristol, TN 37620	000029
Biocraft Laboratories, Inc., 92 Route 46, Elmwood Park, NJ 07407	000032
Biomed Laboratories, 438 West Arrow Highway, Unit 30, San Dimas, CA 91773	051259
Blair Milling & Elevator Co., Inc., 1000 Main St., Atchison, KS 66002	018597
Boehringer Ingelheim Animal Health, Inc., 2621 North Belt Highway, St. Joseph, MO 64502	000010
Bolar Pharmaceutical Co., Inc., 130 Lincoln St., Copiague, NY 11726	000725
Bristol Laboratories, Division of Bristol-Myers Co., P.O. Box 4755, Syracuse, NY 13221-4755	000015
CEVA Laboratories, Inc., 7101 College Blvd., Suite 610, Overland Park, KS 66210	050604
Cardco, Inc., P.O. Box 3599, 10100 Douglas Ave., Des Moines, IA 50322	011490
Cargill, Inc.-Nutrena Feed Div., P.O. Box 9300, Minneapolis, MN 55440	029502
Carnation Co., 5045 Wilshire Blvd., Los Angeles, CA 90036	047019

(1) ALPHABETICAL LISTING OF SPONSORS—Continued

Firm name and address	Drug labeler code
Central Soya Co., Inc., P.O. Box 1400, Fort Wayne, IN 46801-1400	012286
Chemdex, Inc., 12340 Santa Fe Dr., Lenexa, KS 66215	017287
Ciba Pharmaceutical Co., 556 Morris Ave., Summit, NJ 07901	000028
Combe, Inc., 1101 Westchester Ave., White Plains, NY 10604	011509
Cooper U.S.A., Inc., P.O. Box 12338, Research Triangle Park, NC 27709	011482
Cooperative Research Farms, Box 60, Charlotteville, NY 12036	051267
Coopers Animal Health, Inc., Kansas City, KS 66103-1438	017220
John D. Copanos & Co., Inc., Baltimore, MD 21225	010221
Custom Feed Blenders Corp., 540 Hawkeye Ave., Fort Dodge, IA 50501	046987
Custom Feed Services Corp., 2100 N. 13th St., Norfolk, NE 68701	017473
Cutter Laboratories, Inc., Fourth and Parker St., Berkeley, CA 94710	000161
Cyanamid Agricultural de Puerto Rico, Inc., P.O. Box 243, Manati, PR 00701	043781
Dale Atley Co., P.O. Box 444, 222 Sylvan St., St. Joseph, MO 64502	018063
Danbury Pharmaceutical, Inc., 131 West St., Danbury, CT 06810	000591
Dawes Laboratories, Inc., 450 State St., Chicago Heights, IL 60411	024264
DDI Pharmaceuticals, Inc., 518 Logue Ave., Mountain View, CA 94043	024991
Diamond Shamrock Corp., Nutrition & Animal Health Div., 1100 Superior Ave., Cleveland, Ohio 44114	025001
The Dow Chemical Co., P.O. Box 1706, Midland, MI 48640	025700
Drummer Division of Phoenix Pharmaceuticals, Inc., 111 Leaning St., South Hackensack, NJ 07606	052482
DuPont Pharmaceuticals, One Rodney Square, Wilmington, DE 19898	000056
DuPont Pharmaceuticals, Inc., P.O. Box 363, Manati, PR 00701	000590
Elanco Products Co., A Division of Eli Lilly & Co., Lilly Corporate Center, Indianapolis, IN 46285	000986
Elite Chemical Corp., Inc., P.O. Box 1947, Norcross, GA 30091	055025
The Eugene Ingmand Co., Box 22, Red Oak, Iowa 51526	021533
Evisco Pharmaceuticals, An Affiliate of IGI, Inc., Box 209, Harding Hwy., Buena, NJ 08310	017030
Farmers Feed & Supply Co., Ninth St. at Northwestern Tracks, Tipton, IA 52772	043744
Farmers Friend Mineral Co., Inc., 1048 E. Main St., Louisville, KY 40206	030239
Farmland Industries, Inc., Kansas City, MO 64116	021676
Farnam Companies, Inc., 301 West Osborn, Phoenix, AZ 85013-3928	017135
Fasco Mills Co., Box 70, Route 34 East, Mendota, IL 61342	030604
Feed Products, Inc., 1000 West 47th Ave., Denver, CO 80211	013959
Feed Service Co., Inc., 303 Lundin Blvd., P.O. Box 698, Mankato, MN 56001	030641

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(1) ALPHABETICAL LISTING OF SPONSORS— Continued

Firm name and address	Drug labeler code
Feed Specialties Co., Inc., 1877 NE 58th Ave., Des Moines, IA 50313	017274
Fermenta Animal Health Co., 7410 NW Tiffany Springs Parkway, P.O. Box 901350, Kansas City, MO 64190-1350	054273
Fisons plc, Pharmaceutical Division, 12 Derby Rd., Loughborough, Leicestershire, LE11 0BB, England	012525
Fleming Laboratories, Inc., P.O. Box 34384, Charlotte, NC 28234	015565
Forbes Laboratories, 402 West Lakeside St., Madison, WI 53715	032420
Fort Dodge Laboratories, Fort Dodge, IA 50501	000856
Franklin Laboratories, P.O. Box 666, Amarillo, TX 79105	010250
Fromm Laboratories, Inc., Grafton, WI 53024	020112
Furst-McNess Co., Freeport, IL 61032	010439
Gland-O-Lac Co., 1818 Leavenworth St., Omaha, NE 68102	043735
H. Clay Glover Co., Inc., 1001 Franklin Ave., Garden City, NY 11530	010471
Golden Sun Feeds, Inc., 111 South Fifth St., Estherville, IA 51334	021780
Gosch Feed Mill Corp., 540 South St., Lincoln, NE 68501	021798
Good-Life Division of Central Soya Co., Inc., Good-Life Dr., P.O. Box 687, Effingham, IL 62401	021810
Michael Gordon, Inc., P.O. Box 8091, San Fran- cisco, CA 94118	049047
Gougeon Nutrition, Inc., 1676 Cascade Dr., Marion, OH 43302	050972
Grain Processing Corp., Muscatine, IA 52761	022591
Growmark, Inc., 1701 Towanda Ave., Bloomington, IL 61701	020275
G. C. Hanford Manufacturing Co., P.O. Box 1017, Syracuse, NY 13201	010515
Happy Jack, Inc., Snow Hill, NC 28580	023851
Harold Feeds, Inc., P.O. Box 377, Kouts, IN 46347	043727
Henwood Feed Additives, Division of Feed Spe- cialties Co., Inc., 211 Western Rd., Box 577, Lewisburg, OH 45338	026186
Hess & Clark, Inc., Seventh and Orange Sts., Ashtaband, OH 44805	011801
Dox B. Hickam, Inc., Pharmaceuticals, P.O. Box 35413, Houston, TX 77035	000514
Hoechst-Roussel Agri-Vet Co., Route 202-206 North, Somerville, NJ 08876	012799
Hoffmann-La Roche, Inc., Nutley, NJ 07110	000004
Hubbard Milling Co., 424 North Front St., Man- kato, MN 56001	012190
ICI Americas, Inc., Wilmington, DE 19887	011511
I. D. Russell Co. Laboratories, 2463 Harrison, Box 1, Kansas City, MO 64141	017144
I.M.S. Inc., 13619 Industrial Rd., Omaha, NE 68137	050639
Ileri Feeds, Box T, Oneida, IL 61467	037312
Indiana Farm Bureau Cooperative Association, Inc., 120 E. Market St., Indianapolis, IN 46204	021502
International Nutrition, Inc., 6664 "L" St., Omaha, NE 68117	043733
Ivy Laboratories, Inc., 8857 Bond Street, Over- land Park, KS 66214	021641
J. C. Feed Mills, 1050 Sheffield, P.O. Box 224, Waterloo, IA 50704	039741

(1) ALPHABETICAL LISTING OF SPONSORS— Continued

Firm name and address	Drug labeler code
J & R Specialty Supply Co., 310 Second Ave., SW, P.O. Box 506, Waseca, MN 56093	049768
K. C. Pharmacal, Inc., 1310 Atlantic, P.O. Box 7496, North Kansas City, MO 64116	038782
KASCO-EFCO Laboratories, Inc., P.O. Box 730, Hicksville, NY 11802	010516
Kay Dee Feed Co., 1919 Grand Ave., Sioux City, Iowa 51107	026848
Kerber Milling Co., Box 152, 1817 E. Main St., Emmettsburg, IA 50536	029341
Lambert Kay, A Division of Carter-Wallace, Inc., P.O. Box 418, 1/2 Acre Rd., Cranberry, NJ 08512	011614
Land O'Lakes, Inc., Agricultural Services, 2827 Eighth Avenue South, Fort Dodge IA 50501	034500
Lavergne Supplement Co., 1038 Space Park South, Nashville, TN 37211	022422
Dr. LeGear, Inc., 4161 Beck Ave., St. Louis, MO 63116	011950
Lemmon Co., Sellersville, PA 18960	000693
Luitpold Pharmaceuticals, Inc., Animal Health Division, Shirley, NY 11967	010797
Lypho-Med, Inc., 4020 W. Division St., Chicago, IL 60651	000469
M & M Livestock Products Co., Eagle Grove, IA 50533	026282
MAC-PAGE, Inc., 1800 S. Wilson Ave., Dunn, NC 28334	047427
Martox & Moore, Inc., 1503 East Riverside Drive, Indianapolis, IN 46207	027863
Maury Biological Co., Inc., 6109 South Western Ave., Los Angeles, CA 90047	010719
McClellan Laboratories, Inc., 19600 Sixth Ave., Lakeview, CA 92353	043738
McKesson Laboratories, Bridgeport, CT 06602	000022
McNeil Laboratories, Inc., Camp Hill Rd., Fort Washington, PA 19034	000045
Med-Chem Products, Inc., Woburn, MA 01801	053276
Merck Sharp & Dohme Research Laboratories, Division of Merck & Co., Inc., Rahway, NJ 07065	000006
Micro Chemical, Inc., Amarillo, TX 79105	047126
Mobay Corp., Animal Health Division, P.O. Box 390, Shawnee, Mission, KS 66201	000859
Moorman Manufacturing Co., Quincy, IL 62301	021930
Mountain Vitamins, Inc., 400 North Poplar St., P.O. Box 9210, North Little Rock, AR 72119	043734
Music City Supplement Co., 401 Cowan St., Nashville, TN 37202	017519
Natchez Animal Supply Co., 201 John R. Junkin Dr., Natchez, MS 39120	049968
National Dermaceutical Products, Inc., 8749 Surrey Place, Maineville, OH 45039	051268
National Pharmaceutical Mfg. Co., a Division of Barre-National, Inc., 7205 Windsor Blvd., Bal- timore, MD 21207	000570
Neese & Sons, Inc., Box 128, Magazine Rd., Ankeny, IA 50021	024761
Nixon and Co., Kiewitt Plaza, Omaha, NE 68501	043729
Norbrook Laboratories, Ltd., Station Works, Newry BT35 6JP, Northern Ireland	055558
Norco Mills of Norfolk, Inc., P.O. Box 56, Nor- folk, NE 68701	027190
Norden Laboratories, Inc., Lincoln, NE 68501	011519
Norwich Eaton Pharmaceuticals, Inc., P.O. Box 191, Norwich, NY 13815	000149

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(1) ALPHABETICAL LISTING OF SPONSORS—
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Firm name and address	Drug labeler code
Nutra-Blend Corp., P.O. Box 485, Neosho, MO 64850	050566
Nutrus, Inc., Two Brecksville Commons, 6221 Brecksville Rd., Brecksville, OH 44141	051359
Nylos Trading Co., Inc., P.O. Box 2, Route 202, Pomona, NY 10970	027454
The Ohio Farmers Grain and Supply Association, P.O. Box M, Fostoria, OH 44830	026439
Old Monroe Elevator & Supply Co., Inc., Old Monroe, MO 63366	026948
Osborn Laboratories, Inc., 261 and Oak Sts., Le Sueur, MN 56058	012487
Pacific Molasses Co., 333 Market St., Suite 1000, San Francisco, CA 94105	050112
Parke-Davis, Division of Warner-Lambert Co., 201 Tabor Rd., Morris Plains, NJ 07950	000071
Peevey Co., 730 Second Ave. South, Minneapolis, MN 55402	028459
Pennfield Chemical Corp., 14040 Industrial Rd., Omaha, NE 68137	053389
Peter Hand Foundation, 2 East Marleau St., Waukegan, IL 60085	043737
Pfizer, Inc., 235 East 42d St., New York, NY 10017	000069
Pharmacaps, Inc., P.O. Box 547, 1111 Jefferson Ave., Elizabeth, NJ 07207	010888
Pharmaceutical Basics, Inc., 301 South Cherokee St., Denver, CO 80223	000832
Pharmacia Laboratories, Division of Pharmacia, Inc., Piscataway, NJ 08854	000016
Pitman-Moore, Inc., Mundelein, IL 60050	011716
Premier Malt Products, Inc., Milwaukee, WI 53201	032707
Protein Blenders, Inc., Box 631, Highway 218 South, Iowa City, IA 52240	033999
Purina Mills, Inc., P.O. Box 66812, St. Louis, MO 63166-6812	017800
Qazal-Tech Products, Inc., 318 Lake Hazeltine Drive, Chaska, MN 55318	016968
Quality Plus Essar Corp., P.O. Box 459, Fort Dodge, IA 50501	053617
The Rath Packing Co., P.O. Box 330, Waterloo, IA 50704	028260
Rhone-Poulenc, Inc., P.O. Box 125, Black Horse Lane, Monmouth Junction, NJ 08852	011526
Richlyn Laboratories, Inc., Castor and Kensington Aves., Philadelphia, PA 19124	000115
A. H. Robins Co., 1405 Cummings Dr., P.O. Box 26609, Richmond, VA 23261	000031
Roussel-UCLAF, Division Agro-Vetinaire, 163 Avenue Gambetta, 75020 Paris, France	012579
Salsbury Laboratories, Charles City, IA 50616	017210
R. P. Scherer North America, P.O. Box 5800, Clearwater, FL 33618	011014
Schering Corp., Gallop Hill Rd., Kenilworth, NJ 07033	000061
G. D. Searle & Co., P.O. Box 5110, Chicago, IL 60680	000014
Seeco Inc., Box 1014, North Highway 71, Wilmar, MN 56201	011749
Shell Chemical Co., Division of Shell Oil Co., Animal Health, One Shell Plaza, Houston, TX 77001	011461
Shulton Industries, Inc., 221 East Camelback Rd., Suite 21, Phoenix, AZ 85012	052292
Shurjets Co., Inc., 2060 West 15th St., Loveland, Colo. 80537	035999

(1) ALPHABETICAL LISTING OF SPONSORS—
Continued

Firm name and address	Drug labeler code
Simonsen Mill-Rendering Plant, Inc., Quincy, IA 51049	034418
SmithKline Animal Health Products, Division of SmithKline Beecham Corp., 1600 Paoli Pike, West Chester, PA 19380	000007
Solvay Veterinary, Inc., P.O. Box 7348, Princeton, NJ 08540	053501
South St. Paul Feeds, Inc., 500 Farwell Ave., South St. Paul, MN 55075	001860
Southern Micro-Blenders, Inc., 2801 North Hawthorne St., Chattanooga, TN 37406	049885
Springfield Milling Corp., Vigorens Feeds, Springfield, MN 56087	035965
Square Deal Fortification Co., Kouts, IN 48347	036108
Square Laboratories, Inc., 100 Mill St., Revere, MA 02151	017153
Stauffer Chemical Co., 1200 South 47th St., Richmond, CA 94804	017032
Stenis Laboratories, Inc., 620 North 51st Ave., Phoenix, AZ 85043-4705	000402
Sterivof Laboratories, Ltd., 3909 Nashua Dr., Unit 5 Mississauga, ON, Canada L4V 1 R3	047408
Sterling Drug Inc., 90 Park Ave., New York, NY 10016	000934
Stuffs Scientific Service, Inc., P.O. Box 72, Ontario, CA 91762	049896
Summit Hill Laboratories, P.O. Box 535, Navesink, NJ 07752	037990
Syntex Animal Health, Inc., 3401 Hillview Ave., Palo Alto, CA 94304	000033
Tevcon Ind., Inc., 8904 J St., Omaha, NE 68127	011757
Texas Vitamin Co., P.O. Box 18417, 10695 Aledo St., Dallas, TX 75218	000842
TPC Products, Inc., P.O. Box 4308, 2021 North Grove St., Fort Worth, TX 76106	011531
Tulag Pharmaceuticals, Inc., 2599 W. Midway Blvd., Broomfield, CO 80020	000124
Tyson Foods, Inc., S. Johnson Rd., Springdale, AR 72764	035221
United Suppliers, Inc., P.O. Box 538, Eldora, IA 50627	017475
The Upjohn Co., Kalamazoo, MI 49001	000069
V.M.S., Inc., P.O. Box 406, Montgomery, AL 36195-6001	035624
V.P.O., Inc., 4444 S. 78th St., Omaha, NE 68127	043743
VET-A-MIX Laboratories, Inc., P.O. Box 86, Shennandoah, IA 51601	032988
Vetem, S.p.A., Viale E. Bezzi 24, 20146 Milano, Italy	055882
Veterinary Laboratories, Inc., 12340 Santa Fe Dr., Lenexa, KS 66215	000857
Veterinary Service, Inc., 416 North Jefferson St., P.O. Box 2467, Modesto, CA 95354	033008
Vita Plus Corp., 1508 W. Badger Rd., P.O. Box 826, Madison, WI 53701	033071
J. H. Wake Feed Mill, Inc., 402-406 First Avenue West, Osakis, IA 52577	017476
Walnut Grove Products, Division of W. R. Grace & Co., 201 Linn St., Atlantic, IA 50022	034139
Waterloo Mills Co., 2050 Mitchell Ave., Waterloo, Iowa 50704	017139
Wayne Feed Division, Continental Grain Co., P.O. Box 459, Libertyville, IL 60048	034936
Webel Feeds, Inc., R.R. 3, Pittsfield, IL 62363	035098

(1) ALPHABETICAL LISTING OF SPONSORS—
Continued

Firm name and address	Drug labeler code
Wendt Laboratories, Inc., 100 Nancy Dr., Belle Plaine, MN 56011	015579
West Agro, Inc., 11100 N. Congress Ave., Kansas City, MO 64153	033392
Westchester Veterinary Products, Inc., 180 Ma- maroneck Ave., White Plains, NY 10601	043732
Western Serum Co., P.O. Box 7025, Phoenix, AZ 85011	011396
Whitmoyer Laboratories, 19 North Railroad St., Myerstown, PA 17067	011794
Widale Laboratories, Inc., 1401 Duff Dr., Suite 800, Fort Collins, CO 80524	053923
Wyeth Laboratories, Division American Home Products Corp., P.O. Box 8299, Philadelphia, PA 19101	000008
Yoder Feed, Division of Yoder, Inc., Kalona, IA 52247	035369
Young's Inc., Roaring Spring, PA 16673	035393
Zema Corp., P.O. Box 12903, Research Trian- gle Park, Durham, NC 27709	050906
Zenith Laboratories, Inc., 50 Williams Dr., Ramsey, NJ 07446	000172
Zocon Industries, Inc., 12200 Denton Dr., Dallas, Tex. 75234	011536

(2) NUMERICAL LISTING OF SPONSORS

Drug labeler code	Firm name and address
000004	Hoffmann-La Roche, Inc., Nutley, NJ 07110
000006	Merck Sharp & Dohme Research Laborato- ries, Division of Merck & Co., Inc., Rahway, NJ 07065
000007	SmithKline Animal Health Products, Divi- sion of SmithKline, Beckman Corp., 1600 Paoli Pike, West Chester, PA 19380
000008	Wyeth Laboratories, Division American Home Products Corp., P.O. Box 8299, Philadelphia, PA 19101
000009	The Upjohn Co., Kalamazoo, MI 49001
000010	Boehringer Ingelheim Animal Health, Inc., 2621 North Belt Highway, St. Joseph, MO 64502
000014	G. D. Searle & Co., P.O. Box 5110, Chic- ago, IL 60680
000015	Bristol Laboratories, Division of Bristol- Myers Co., P.O. Box 4755, Syracuse, NY 13221-4755
000016	Pharmacia Laboratories, Division of Phar- macia, Inc., Piscataway, NJ 08854
000022	McKesson Laboratories, Bridgeport, CT 06602
000028	Ciba Pharmaceutical Co., 556 Morris Ave., Summit, NJ 07901
000029	Beecham Laboratories, Division of Bee- cham Inc., Bristol, TN 37620
000031	A. H. Robins Co., 1405 Cummings Dr., P.O. Box 26808, Richmond, VA 23261
000033	Syntex Animal Health, Inc., 3401 Hillview Ave., Palo Alto, CA 94304
000045	McNeil Laboratories, Inc., Camp Hill Rd., Fort Washington, PA 19034

(2) NUMERICAL LISTING OF SPONSORS—
Continued

Drug labeler code	Firm name and address
000046	Ayerst Laboratories, Division of American Home Products Corp., 685 Third Ave., New York, NY 10017
000056	DuPont Pharmaceuticals, One Rodney Square, Wilmington, DE 19886
000061	Schering Corp., Galloping Hill Rd., Kenil- worth, NJ 07033
000069	Pfizer, Inc., 235 East 42d St., New York, NY 10017
000071	Parke-Davis, Division of Warner-Lambert Co., 201 Tabor Rd., Morris Plains, NJ 07950
000115	Pchlyn Laboratories, Inc., Castor and Ken- sington Aves., Philadelphia, PA 19124
000124	Tutag Pharmaceuticals, Inc., 2599 W. Midway Blvd., Broomfield, CO 80020
000138	American Scientific Laboratories, A Division of Schering Corp., Bloomfield, NJ 07003
000149	Norwich Easton Pharmaceuticals, Inc., P.O. Box 191, Norwich, NY 13815
000161	Cutter Laboratories, Inc., Fourth and Parker St., Berkeley, CA 94710
000172	Zenith Laboratories, Inc., 50 Williams Dr., Ramsey, NJ 07446
000332	Biocraft Laboratories, Inc., 92 Route 46, Elmwood Park, NJ 07407
000402	Stern Laboratories, Inc., 620 North 51st Ave., Phoenix, AZ 85043-4705
000469	Lypho-Med, Inc., 4020 W. Division St., Chi- cago, IL 60651
000514	Dow B. Hickam, Inc., Pharmaceuticals, P.O. Box 35413, Houston, TX 77035
000570	National Pharmaceutical Mfg. Co., a Divi- sion of Bama-National, Inc., 7205 Wind- sor Blvd., Baltimore, MD 21207
000590	DuPont Pharmaceuticals, Inc., P.O. Box 363, Manas, PR 00701
000591	Danbury Pharmacal, Inc., 131 West St., Danbury, CT 06810
000683	Lemmon Co., Sellersville, PA 18960
000725	Binar Pharmaceutical Co., Inc., 130 Lincoln St., Copiague, N.Y. 11726
000794	S. B. Penick & Co., 1050 Wall St. West, Lyndhurst, NJ 07071
000832	Pharmaceutical Basics, Inc., 301 South Cherokee St., Denver, CO 80223
000842	Texas Vitamin Co., P.O. Box 18417, 10695 Aledo St., Dallas, TX 75218
000856	Fort Dodge Laboratories, Fort Dodge, IA 50501
000857	Veterinary Laboratories, Inc., 12340 Santa Fe Dr., Lenexa, KS 66215
000859	Mobay Corp., Animal Health Division, P.O. Box 390, Shawnee, Mission, KS 66201
000864	Anthony Products Co., 5600 Peck Rd., Ar- cadia, CA 91006
000934	Sterling Drug Inc., 90 Park Ave., New York, NY 10016
000986	Elianco Products Co., A Division of Eli Lilly & Co., Lilly Corporate Center, Indianapo- lis, IN 46285
001800	South St. Paul Feeds, Inc., 520 Farwell Ave., South St. Paul, MN 55075
010019	Anaquest, a Division of BOC, Inc., 100 Mountain Ave., Murray Hill, NJ 07974
010042	American Cyanamid Co., Berdan Ave., Wayne, NJ 07470

(2) NUMERICAL LISTING OF SPONSORS—
Continued

Drug labeler code	Firm name and address
010271	John D. Copence & Co., Inc., Baltimore, MD 21225.
010290	Franklin Laboratories, P.O. Box 669, Amarillo, TX 79105.
010439	Furst-McNess Co., Freeport, IL 61032.
010471	H. Clay Glover Co., Inc., 1001 Franklin Ave., Garden City, NY 11530.
010515	G. C. Hartford Manufacturing Co., P.O. Box 1017, Syracuse, NY 13201.
010616	KASCO-EFCO Laboratories, Inc., P.O. Box 730, Hicksville, NY 11802.
010719	Maury Biological Co., Inc., 6109 South Western Ave., Los Angeles, CA 90047.
010797	Luitpold Pharmaceuticals, Inc., Animal Health Division, Shirley, NY 11967.
010888	Pharamcaps, Inc., P.O. Box 547, 1111 Jefferson Ave., Elizabeth, NJ 07207.
011014	R. P. Scherer North America, P.O. Box 5600, Clearwater, FL 33518.
011398	Western Serum Co., P.O. Box 7025, Phoenix, AZ 85011.
011461	Shell Chemical Co., Division of Shell Oil Co., Animal Health, One Shell Plaza, Houston, TX 77001.
011485	Albion Laboratories, Inc., 101 North Main, Clearfield, UT 84015.
011490	Cadco, Inc., P.O. Box 3599, 10100 Douglas Ave., Des Moines, IA 50322.
011492	Cooper U.S.A., Inc., P.O. Box 12338, Research Triangle Park, NC 27709.
011509	Combe, Inc., 1101 Westchester Ave., White Plains, NY 10604.
011511	ICI Americas, Inc., Wilmington, DE 19887.
011519	Norden Laboratories, Inc., Lincoln, NE 68501.
011526	Rhone-Poulenc, Inc., P.O. Box 125, Black Horse Lane, Monmouth Junction, NJ 08852.
011531	TPC Products, Inc., P.O. Box 4308, 2021 North Grove St., Fort Worth, TX 76106.
011536	Zoecon Industries, Inc., 12200 Denton Dr., Dallas, TX 75234.
011614	Lambert Kay, a Division of Carter-Wallace, Inc., P.O. Box 418, 1/2 Acre Rd., Cranberry, NJ 08512.
011716	Pitman-Moore, Inc., Mundelein, IL 60060.
011749	Seeco Inc., Box 1014, North Highway 71, Willmar, MN 56201.
011794	Whitmoyer Laboratories, 19 North Railroad St., Myerstown, PA 19067.
011801	Heitz & Clark, Inc., Seventh and Orange Sts., Ashland, OH 44805.
011825	Affiliated Laboratories Division, Whitmoyer Laboratories, Inc., 19 North Railroad St., Myerstown, PA 19067.
011950	Dr. LeGear, Inc., 4181 Beck Ave., St. Louis, MO 63116.
012190	Hubbard Milling Co., 424 North Front St., Mankato, MN 56001.
012286	Central Soya Co., Inc., P.O. Box 1400, Fort Wayne, IN 46801-1400.
012487	Osborn Laboratories, Inc., 2d and Oak Sts., Le Sueur, MN 56058.
012525	Fisons plc, Pharmaceutical Division, 12 Derby Rd., Loughborough, Leicestershire, LE11 0BB, England.

(2) NUMERICAL LISTING OF SPONSORS—
Continued

Drug labeler code	Firm name and address
012579	Roussel-UCLAF, Division Agro-Vetinaire, 163 Avenue Gambetta, 75020 Paris, France.
012789	Hoechst-Roussel Agri-Vet Co., Route 202-206 North, Somerville, NJ 08876.
012983	Allied Pharmaceutical, Division of K. C. Pharmaceutical, Inc., 1234 Clay St., North Kansas City, MO 64116.
013959	Feed Products, Inc., 1000 West 47th Ave., Denver, CO 80211.
015563	Agribusiness Marketers, Inc., 2667 West Dual, Baton Rouge, LA 70815.
015565	Fleming Laboratories, Inc., P.O. Box 34384, Charlotte, NC 28234.
015579	Wendt Laboratories, Inc., 100 Nancy Dr., Belle Plaine, MN 56011.
018968	Quali-Tech Products, Inc., 318 Lake Hazlet Dr., Chaska, MN 55318.
017030	Evco Pharmaceuticals, An Affiliate of IGI, Inc., Box 209, Harding Hwy., Buena, NJ 08310.
017032	Stauffer Chemical Co., 1200 South 47th St., Richmond, CA 94804.
017135	Farnam Companies, Inc., 301 West Osborn, Phoenix, AZ 85013-3928.
017139	Waterloo Mills Co., 2050 Mitchell Ave., Waterloo, IA 50704.
017144	I. D. Russell Co. Laboratories, 2463 Harrison, Box 1, Kansas City, MO 64141.
017153	Squire Laboratories, Inc., 100 Mill St., Revere, MA 02151.
017210	Salsbury Laboratories, Charles City, IA 50616.
017220	Coopers Animal Health, Inc., Kansas City, KS 66103-1438.
017274	Feed Specialties Co., Inc., 1877 Northeast 58th Ave., Des Moines, IA 50313.
017287	Chemdex, Inc., 12340 Santa Fe Dr., Lenexa, KS 66215.
017473	Custom Feed Services Corp., 2100 N. 13th St., Norfolk, NE 68701.
017475	United Suppliers, Inc., P.O. Box 538, Eldora, IA 50627.
017476	J. H. Wake Feed Mill, Inc., 402-406 First Avenue West, Oskaloosa, IA 52577.
017519	Music City Supplement Co., 401 Cowan St., Nashville, TN 37202.
017762	Agri-Tech, Inc., 4722 Broadway, Kansas City, MO 64112.
017790	Carl S. Akey, Inc., P.O. Box 607, Lewisburg, OH 45338.
017800	Purina Mills, Inc., P.O. Box 66812, St. Louis, MO 63166-6812.
017826	Albers Milling Co., Carnation Bldg., 5045 Wilshire Blvd., Los Angeles, CA 90036.
018083	Dale Alley Co., P.O. Box 444, 222 Sylvan St., St. Joseph, MO 64502.
018597	Blair Milling & Elevator Co., Inc., 1000 Main St., Atchison, KS 66002.
020275	Growmark, Inc., 1701 Towanda Ave., Bloomington, IL 61701.
020112	Fromm Laboratories, Inc., Grafton, WI 53024.
021188	Babineaux's Veterinary Products, Inc., 6425 Airline Highway, Metairie, LA 70003.
021502	Indiana Farm Bureau Cooperative Association, Inc., 120 E. Market St., Indianapolis, IN 46204.

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(2) NUMERICAL LISTING OF SPONSORS— Continued

Drug labeler code	Firm name and address
021533	The Eugene Ingmand Co., Box 22, Red Oak, IA 51566.
021841	Ivy Laboratories, Inc., 8857 Bond Street, Overland Park, KS 66214.
021876	Farmland Industries, Inc., Kansas City, MO 64116.
021780	Golden Sun Feeds, Inc., 111 South Fifth St., Estherville, IA 51334.
021798	Gooch Feed Mill Corp., 540 South St., Lincoln, NE 68501.
021810	Good-Life Division of Central Soya Co., Inc., Good-Life Dr., P.O. Box 687, El-fingham, IL 62401.
021830	Moorman Manufacturing Co., Quincy, IL 62301.
022422	Laverne Supplement Co., 1038 Space Park South, Nashville, TN 37211.
022591	Gran Processing Corp., Muscatine, IA 52761.
023368	Agri-Basics, ConAgra-Westfeeds, 1420 Minnesota Ave, Billings, MT 59101.
023851	Happy Jack, Inc., Snow Hill, NC 28580.
024174	Ag-Mark, Inc., P.O. Box 127, Teachey, NC 28454.
024254	Dawes Laboratories, Inc., 450 State St., Chicago Heights, IL 60411.
024751	Neese & Sons, Inc., Box 128, Magazine Rd., Ankeny, IA 50021.
024981	DDI Pharmaceuticals, Inc., 518 Logue Ave., Mountain View, CA 94043.
025001	Diamond Shamrock Corp., Nutrition & Animal Health Div., 1100 Superior Ave., Cleveland, OH 44114.
025463	Altana Inc., 80 Baylis Rd., Melville, NY 11747.
025700	The Dow Chemical Co., P.O. Box 1706, Midland, MI 48640.
026186	Hemwood Feed Additives, Division of Feed Specialties Co., Inc., 211 Western Rd., Box 577, Lewisburg, OH 45338.
026282	M & M Livestock Products Co., Eagle Grove, IA 50533.
026439	The Ohio Farmers Grain and Supply Association, P.O. Box M, Fostoria, OH 44830.
026648	Kay Dee Feed Co., 1919 Grand Ave., Sioux City, Iowa 51107.
026948	Old Monroe Elevator & Supply Co., Inc., Old Monroe, MO 63369.
027190	Norco Mills of Norfolk, Inc., P.O. Box 56, Norfolk, NE 68701.
027454	Nylos Trading Co., Inc., P.O. Box 2, Route 202, Pomona, NY 10970.
027863	Mattox & Moore, Inc., 1503 East Riverside Dr., Indianapolis, IN 46207.
028260	The Rath Packing Co., P.O. Box 330, Waterloo, IA 50704.
028459	Peavey Co., 730 Second Ave. South, Minneapolis, MN 55402.
029341	Kerber Milling Co., Box 152, 1817 E. Main St., Emmetsburg, IA 50536.
030029	Farmers Friend Mineral Co., Inc., 1048 E. Main St., Louisville, KY 40206.
030804	Fasco Mills Co., Box 70, Route 34 East, Mendota, IL 61342.
030841	Feed Service Co., Inc., 303 Lundin Blvd., P.O. Box 696, Menkato, MN 56001.
030420	Forbes Laboratories, 402 West Lakeside St., Madison, WI 53715.

(2) NUMERICAL LISTING OF SPONSORS— Continued

Drug labeler code	Firm name and address
032707	Premier Malt Products, Inc., Milwaukee, WI 53201.
032998	VET-A-MIX Laboratories, Inc., P.O. Box 86, Shenandoah, IA 51801.
033008	Veterinary Service, Inc., 416 North Jefferson St., P.O. Box 2467, Modesto, CA 95354.
033071	Vita Plus Corp., 1506 West Badger Rd., P.O. Box 926, Madison, WI 53701.
033392	West Agro, Inc., 11100 N. Congress Ave., Kansas City, MO 64153.
033999	Protein Blenders, Inc., Box 631, Highway 218 South, Iowa City, IA 52240.
034139	Walnut Grove Products, Division of W. R. Grace & Co., 201 Linn St., Atlantic, IA 50022.
034418	Simonsen Mill-Rendering Plant, Inc., Quamby, IA 51049.
034500	Land O'Lakes, Inc., Agricultural Services, 2827 Eighth Avenue South, Fort Dodge, IA 50501.
034936	Wayne Feed Division, Continental Grain Co., P.O. Box 459, Libertyville, IL 60048.
035098	Weibel Feeds, Inc., R.R. 3, Pittsfield, IL 62363.
035221	Tyson Foods, Inc., S. Johnson Rd., Springdale, AR 72764.
035380	Yoder Feed, Division of Yoder, Inc., Kalona, IA 52247.
035393	Young's, Inc., Roaring Spring, PA 16673.
035624	V.M.S., Inc., P.O. Box 406, Montgomery, AL 36195-8001.
035955	Springfield Milling Corp., Vigorena Feeds, Springfield, MN 56087.
035999	Shurjets Co., Inc., 2080 West 15th St., Loveland, Colo. 80537.
036108	Square Deal Fortification Co., Kouts, IN 46347.
037310	Ilini Feeds, Box T, Oneida, IL 61467.
037990	Summit Hill Laboratories, P.O. Box 535, Navesink, NJ 07752.
038782	K. C. Pharmacal, Inc., 1310 Atlantic, P.O. Box 7496, North Kansas City, MO 64116.
039502	Cargill, Inc.-Nutrena Feed Div., P.O. Box 9300, Minneapolis, MN 55440.
039741	J. C. Feed Mills, 1050 Sheffield, P.O. Box 224, Waterloo, IA 50704.
043727	Heinold Feeds, Inc., P.O. Box 377, Kouts, IN 46347.
043728	Balfour Guthrie & Co., Ltd., 315 North H St., Fresno, CA 93701.
043729	Nixon and Co., Kiewitt Plaza, Omaha, NE 68501.
043731	Abbott Laboratories, North Chicago, IL 60064.
043732	Westchester Veterinary Products, Inc., 180 Mamaroneck Ave., White Plains, NY 10601.
043733	International Nutrition, Inc., 6664 L St., Omaha, NE 68117.
043734	Mountaire Vitamins, Inc., 400 North Poplar St., P.O. Box 9210, North Little Rock, AR 72119.
043735	Gland-O-Lac Co., 1818 Leavenworth St., Omaha, NE 68102.
043737	Peter Hand Foundation, 2 East Madison St., Waukegan, IL 60085.

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(2) NUMERICAL LISTING OF SPONSORS— Continued

Drug labeler code	Firm name and address
043738	McClellan Laboratories, Inc., 19600 Sixth Ave., Lakeview, CA 92353.
043743	V.P.O., Inc., 4444 South 76th St., Omaha, NE 68127.
043744	Farmers Feed & Supply Co., Ninth St. at Northwestern Tracks, Tipton, IA 52772.
043781	Cyanamid Agricultural de Puerto Rico, Inc., P.O. Box 243, Manati, PR 00701.
048573	A. L. Laboratories, Inc., A Subsidiary of A/S Apothekernes Laboratorium for Special-præparater, One Executive Drive, P.O. Box 1399, Fort Lee, NJ 07024.
048987	Custom Feed Blenders Corp., 540 Hawk-eyes Ave., Fort Dodge, IA 50501.
047019	Carnation Co., 5045 Wilshire Blvd., Los Angeles, CA 90036.
047126	Micro Chemical, Inc., Amarillo, TX 79105.
047408	Stervet Laboratories, Ltd., 3909 Nashua Dr., Unit 5 Mississauga, ON, Canada L4V 1 R3.
047427	MAC-PAGE, Inc., 1600 S. Wilson Ave., Dunn, NC 28334.
047863	Arkansas Micro Specialties Inc., P.O. Box 308, Highway 71 North, Lowell, AR 72745.
048696	Stutts Scientific Service, Inc., P.O. Box 72, Ontario, CA 91762.
049047	Michael Gordon, Inc., P.O. Box 1091, San Francisco, CA 94118.
049685	Southern Micro-Blenders, Inc., 3801 North Hawthorne St., Chattanooga, TN 37406.
049768	J & R Specialty Supply Co., 310 Second Ave., SW., P.O. Box 506, Waseca, MN 56093.
049968	Natchez Animal Supply Co., 201 John R. Junkin Dr., Natchez, MS 39120.
050112	Pacific Molasses Co., 333 Market St., Suite 1000, San Francisco, CA 94105.
050568	Nutra-Blend Corp., P.O. Box 485, Neosho, MO 64850.
050604	CEVA Laboratories, Inc., 7101 College Blvd., Suite 610, Overland Park, KS 66210.
050639	I.M.S. Inc., 13619 Industrial Rd., Omaha, NE 68137.
050906	Zema Corp., P.O. Box 12903, Research Triangle Park, Durham, NC 27709.
050972	Gossell Nutrition, Inc., 1676 Cascade Dr., Marion, OH 43302.
051212	Argent Laboratories, 8702 152d Ave. NE., Redmond, WA 98052.
051259	Biomed Laboratories, 438 West Arrow Highway, Unit 30, San Dimas, CA 91773.
051267	Cooperative Research Farms, Box 69, Charlottesville, NY 12036.
051268	National Dermaceutical Products, Inc., 8749 Surrey Place, Maineville, OH 45099.
051359	Nutrus, Inc., Two Brecksville Commons, 8221 Brecksville Rd., Brecksville, OH 44141.
052292	Shulcon Industries, Inc., 221 East Camel-back Rd., Suite 21, Phoenix, AZ 85012.
052492	Drummer Division of Phoenix Pharmaceuticals, Inc., 111 Leaning St., South Hackensack, NJ 07606.
054276	Med-Chem Products, Inc., Woburn, MA 01801.

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(2) NUMERICAL LISTING OF SPONSORS— Continued

Drug labeler code	Firm name and address
053389	Pennfield Chemical Corp., 14040 Industrial Rd., Omaha, NE 68137.
053501	Solvay Veterinary, Inc., P.O. Box 7348, Princeton, NJ 08540.
053617	Quality Plus Essar Corp., P.O. Box 459, Fort Dodge, IA 50501.
053923	Wildlife Laboratories, Inc., 1401 Duff Dr., Suite 600, Fort Collins, CO 80524.
054273	Farmenia Animal Health Co., 7410 NW Tiffany Springs Parkway, P.O. Box 901350, Kansas City, MO 64190-1350.
055025	Elite Chemical Corp., Inc., P.O. Box 1947, Norcross, GA 30091.
055558	Norbrook Laboratories, Ltd., Station Works, Newry BT35 6JP, Northern Ireland.
055882	Vetam, S.p.A., Viale E. Bezzi 24, 20146 Milano, Italy.

[40 FR 13807, Mar. 27, 1975]

EDITORIAL NOTE: For FEDERAL REGISTER citations affecting § 510.600, see the List of CFR Sections Affected in the Finding Aids section of this volume.

PART 511—NEW ANIMAL DRUGS FOR INVESTIGATIONAL USE

§ 511.1 New animal drugs for investigational use exempt from section 512(a) of the act.

(a) *New animal drugs for tests in vitro and in laboratory research animals.* (1) A shipment or other delivery of a new animal drug or animal feed bearing or containing a new animal drug intended solely for tests in vitro or in animals used only for laboratory research purposes shall be exempt from section 512 (a) and (m) of the act if it is labeled as follows:

Caution. Contains a new animal drug for investigational use only in laboratory research animals or for tests in vitro. Not for use in humans.

(2) The person distributing or causing the distribution of new animal drugs for tests in vitro or in animals used only for laboratory research purposes under this exemption shall use due diligence to assure that the consignee is regularly engaged in conducting such tests and that the shipment of the new animal drug will actually be used for tests in vitro or in animals used only for laboratory research.

(3) The person who introduced such shipment or who delivered the new animal drug for introduction into interstate commerce shall maintain adequate records showing the name and post office address of the expert or expert organization to whom the new animal drug is shipped and the date, quantity, and batch or code mark of each shipment and delivery for a period of 2 years after such shipment and delivery. Upon the request of a properly authorized employee of the Department at reasonable times, he shall make such records available for inspection and copying.

(4) The exemption allowed in this paragraph shall not apply to any new animal drug intended for in vitro use in the regular course of diagnosing or treating disease, including antibacterial sensitivity discs impregnated with any new animal drug or drugs, which discs are intended for use in determining susceptibility of microorganisms to the new animal drug or drugs.

(b) *New animal drugs for clinical investigation in animals.* A shipment or other delivery of a new animal drug or an animal feed containing a new animal drug intended for clinical investigational use in animals shall be exempt from section 512(a) and (m) of the act if all the following conditions are met:

(1) The label shall bear the statements:

Caution. Contains a new animal drug for use only in investigational animals in clinical trials. Not for use in humans. Edible products of investigational animals are not to be used for food unless authorization has been granted by the U.S. Food and Drug Administration or by the U.S. Department of Agriculture.

In the case of containers too small or otherwise unable to accommodate a label with sufficient space to bear the caution statements required by paragraph (a) or (b) of this section, the statements may be included on the carton label and other labeling on or within the package from which the new animal drug is to be dispensed.

(2) The person or firm distributing or causing the distribution of the new animal drug or animal feed containing new animal drug shall use due diligence to assure that the new animal

drug or animal feed containing a new animal drug will actually be used for tests in animals and is not used in humans.

(3) The person who introduced such shipment or who delivered the new animal drug or animal feed containing a new animal drug for introduction into interstate commerce shall maintain adequate records showing the name and post office address of the investigator to whom the new animal drug or animal feed containing a new animal drug is shipped and the date, quantity, and batch or code mark of each shipment and delivery for a period of 2 years after such shipment and delivery. Upon the request of a properly authorized employee of the Department at reasonable times, such records shall be made available for inspection and copying.

(4) Prior to shipment of the new animal drug for clinical tests in animals, the sponsor of the investigation shall submit in triplicate to the Food and Drug Administration a "Notice of Claimed Investigational Exemption for a New Animal Drug" including a signed statement containing the following information:

(i) The identity of the new animal drug.

(ii) All labeling and other pertinent information to be supplied to the investigators. When such pertinent information includes nonclinical laboratory studies, the information shall include, with respect to each nonclinical study, either a statement that the study was conducted in compliance with the requirements set forth in Part 58 of this chapter, or, if the study was not conducted in compliance with such regulations, a brief statement of the reason for the noncompliance.

(iii) The name and address of each clinical investigator.

(iv) The approximate number of animals to be treated (or if not available, the amount of new animal drug to be shipped).

(v) If the new animal drug is given to food-producing animals, the statement shall contain the following additional information:

(a) A commitment that the edible products from such animals shall not be used for food without prior authori-

zation in accordance with the provisions prescribed in this section.

(b) Approximate dates of the beginning and end of the experiment or series of experiments.

(c) The maximum daily dose(s) to be administered to a given species, the size of animal, maximum duration of administration, method(s) of administration, and proposed withdrawal time, if any.

(vi) If a sponsor has transferred any obligations for the conduct of any clinical study to a contract research organization, a statement containing the name and address of the contract research organization, identification of the clinical study, and a listing of the obligations transferred. If all obligations governing the conduct of the study have been transferred, a general statement of this transfer—in lieu of a listing of the specific obligations transferred—may be submitted.

(5) Authorization for use of edible products derived from a treated food-producing animal may be granted under the provisions of this section and when the following specified conditions are met, except that in the case of an animal administered any unlicensed experimental veterinary biological product regulated under the viruses, serums, toxins statute (21 U.S.C., Chapter V, sec. 151 et seq.) the product shall be exempt from the requirements of this section when U.S. Department of Agriculture approval has been obtained as provided in 9 CFR 103.2. Conditional authorization may be granted in advance of identification of the name(s) and address(es) of the clinical investigator(s) as required by paragraph (b)(4)(iii) of this section. Information required for authorization shall include, in addition to all other requirements of this section, the following:

(i) Data to show that consumption of food derived from animals treated at the maximum levels with the minimum withdrawal periods, if any, specified in accordance with paragraph (b)(4)(v)(c) of this section, will not be inconsistent with the public health; or

(ii) Data to show that food derived from animals treated at the maximum levels and with the minimum withdrawal periods, if any, specified in ac-

cordance with paragraph (b)(4)(v)(c) of this section, does not contain drug residues or metabolites.

(iii) The name and location of the packing plant where the animals will be processed, except that this requirement may be waived, on request, by the terms of the authorization.

Authorizations granted under this paragraph do not exempt investigational animals and their products from compliance with other applicable inspection requirements. Any person who contests a refusal to grant such authorization shall have an opportunity for a regulatory hearing before the Food and Drug Administration pursuant to Part 16 of this chapter.

(6) On written request of the Food and Drug Administration, the sponsor shall submit any additional information reported to or otherwise received by him with respect to the investigation deemed necessary to facilitate a determination whether there are grounds in the interest of public health for terminating the exemption.

(7) The sponsor shall assure himself that the new animal drug is shipped only to investigators who:

(i) Are qualified by scientific training and/or experience to evaluate the safety and/or effectiveness of the new animal drug.

(ii) Shall maintain complete records of the investigations, including complete records of the receipt and disposition of each shipment or delivery of the new animal drug under investigation. Copies of all records of the investigation shall be retained by the investigator for 2 years after the termination of the investigation or approval of a new animal drug application.

(iii) Shall furnish adequate and timely reports of the investigation to the sponsor.

(8) The sponsor:

(i) Shall retain all reports received from investigators for 2 years after the termination of the investigation or approval of a new animal drug application and make such reports available to a duly authorized employee of the Department for inspection at all reasonable times.

(ii) Shall provide for current monitoring of the investigation by a person

qualified by scientific training and experience to evaluate information obtained from the investigation, and shall promptly investigate and report to the Food and Drug Administration and to all investigators any findings associated with use of the new animal drug that may suggest significant hazards pertinent to the safety of the new animal drug.

(iii) Shall not unduly prolong distribution of the new animal drug for investigational use.

(iv) Shall not, nor shall any person acting for or on behalf of the sponsor, represent that the new animal drug is safe or effective for the purposes for which it is under investigation. This requirement is not intended to restrict the full exchange of scientific information.

(v) Shall not commercially distribute nor test-market the new animal drug until a new animal drug application is approved pursuant to section 512(c) of the act.

(9) If the shipment or other delivery of the new animal drug is imported or offered for importation into the United States for clinical investigational use in animals, it shall also meet the following conditions:

(i) The importer of all such shipments or deliveries is an agent of the foreign exporter residing in the United States or the ultimate consignee, which person has, prior to such shipments and deliveries, informed the Food and Drug Administration of his intention to import the new animal drug as sponsor in compliance with the conditions prescribed in this subdivision; or

(ii) The new animal drug is shipped directly to a scientific institution with adequate facilities and qualified personnel to conduct laboratory or clinical investigations and is intended solely for use in such institutions and which institution has submitted a statement as sponsor of the investigation.

(10) The sponsor shall submit either a claim for categorical exclusion under § 25.24 of this chapter or an environmental assessment under § 25.31 of this chapter.

(c) *Withdrawal of eligibility to receive investigational-use new animal*

drugs. (1) Whenever the Food and Drug Administration has information indicating that an investigator has repeatedly or deliberately failed to comply with the conditions of these exempting regulations or has submitted false information either to the sponsor of the investigation or in any required report, the Bureau of Veterinary Medicine will furnish the investigator written notice of the matter complained of in general terms and offer him an opportunity to explain the matter in an informal conference and/or in writing. If an explanation is offered but not accepted by the Bureau of Veterinary Medicine, the investigator shall have an opportunity for a regulatory hearing before the Food and Drug Administration pursuant to Part 16 of this chapter on the question of whether the investigator is entitled to receive investigational new animal drugs.

(2) If, after evaluating all available information, including any explanation presented by the investigator, the Commissioner determines that the investigator has repeatedly or deliberately failed to comply with the conditions of the exempting regulations in this section or has repeatedly or deliberately submitted false information to the sponsor of an investigation, the Commissioner will notify the investigator and the sponsor of any investigation in which he has been named as a participant that the investigator is not entitled to receive investigational use new animal drugs with a statement of the basis for such determination.

(3) Each "Notice of Claimed Investigational Exemption for a New Animal Drug" and each approved new animal drug application containing data reported by an investigator who has been determined to be ineligible to receive investigational-use new animal drugs will be examined to determine whether he has submitted unreliable data that are essential to the continuation of the investigation or essential to the approval of any new animal drug application.

(4) If the Commissioner determines, after the unreliable data submitted by the investigator are eliminated from consideration, that the data remaining are inadequate to support a conclusion

that it is reasonably safe to continue the investigation, he shall first notify the sponsor, who shall have an opportunity for a regulatory hearing before the Food and Drug Administration pursuant to Part 16 of this chapter on whether the exemption should be terminated. If a danger to the public health exists, however, he shall terminate the exemption forthwith and notify the sponsor of the termination. In such event the sponsor shall have an opportunity for a regulatory hearing before the Food and Drug Administration pursuant to Part 16 (see 42 FR 15675, March 22, 1977) of this chapter on the question of whether the exemption should be reinstated.

(5) If the Commissioner determines, after the unreliable data submitted by the investigator are eliminated from consideration, that the data remaining are such that a new animal drug application would not have been approved, he will proceed to withdraw approval of the application in accordance with section 512(e) of the act.

(6) An investigator who has been determined to be ineligible may be reinstated as eligible to receive investigational-use new animal drugs when the Commissioner determines that he has presented adequate assurance that he will employ such new animal drugs solely in compliance with the exempting regulations in this section for investigational-use new animal drugs.

(d) *Termination of exemption.* If the Commissioner finds that:

(1) The sponsor of the investigation has failed to comply with any of the conditions for the exemption established under this section, or

(2) The continuance of the investigation is unsafe or otherwise contrary to the public interest or the drug is being or has been used for purposes other than bona fide scientific investigation, he shall first notify the sponsor and invite his immediate correction. If the conditions of the exemption are not immediately met, the sponsor shall have an opportunity for a regulatory hearing before the Food and Drug Administration pursuant of Part 16 of this chapter on whether the exemption should be terminated. If the exemption is terminated the sponsor shall recall or have destroyed the

unused supplies of the new animal drug.

(e) *Statements and requests.* "Notice(s) of Claimed Investigational Exemption for a New Animal Drug" and requests for authorization to use investigational animals and their products for food should be addressed to the Department of Health and Human Services, Food and Drug Administration, Bureau of Veterinary Medicine, 5600 Fishers Lane, Rockville, MD 20857.

(f) *Contract research organizations.* (1) For purposes of this part and Part 514, "contract research organization" means a person that assumes, as an independent contractor with the sponsor, one or more of the obligations of a sponsor, e.g., design of a protocol, selection or monitoring of investigations, evaluation of reports, and preparation of materials to be submitted to the Food and Drug Administration.

(2) A sponsor may transfer responsibility for any or all of the obligations set forth in this part to a contract research organization. Any such transfer shall be in writing and, if not all obligations are transferred, shall describe each of the obligations being assumed by the contract research organization. If all obligations are transferred, a general statement that all obligations have been transferred is acceptable. Any obligation not covered by the written description shall be deemed not to have been transferred.

(3) A contract research organization that assumes any obligation of a sponsor shall comply with the specific regulations in this chapter applicable to this obligation and shall be subject to the same regulatory action as a sponsor for failure to comply with any obligation assumed under these regulations. Thus, all references to "sponsor" in this part apply to a contract research organization to the extent that it assumes one or more obligations of the sponsor.

(Secs. 406, 408, 409, 501, 502, 503, 505, 506, 507, 510, 512-516, 518-520, 601, 701, 706, and 801, 52 Stat. 1049-1053 as amended, 1055, 1056 as amended, 1058 as amended, 55 Stat. 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511-517 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 399-407 as amended, 76 Stat. 794 as amended, 82 Stat. 343-351, 90

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Stat. 539-574 (21 U.S.C. 346, 346a, 348, 351, 352, 353, 355, 356, 357, 360, 360b-360f, 360h-360i, 371, 376); secs. 215, 301, 351, 354-360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 241, 262, 263b-263n)

(40 FR 13823, Mar. 27, 1975, as amended at 41 FR 46268, Nov. 2, 1976; 42 FR 15675, Mar. 22, 1977; 50 FR 7517, Feb. 22, 1985; 50 FR 16668, Apr. 28, 1985; 52 FR 8847, Mar. 19, 1987)

PART 514—NEW ANIMAL DRUG APPLICATIONS

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AUTHORITY: Secs. 512(i), (n), 701(a), 52 Stat. 1955; 82 Stat. 343-351 (21 U.S.C. 360b(i), (n), 371(a)); 21 CFR 5.10, 5.11.

SOURCE: 40 FR 13825, Mar. 27, 1975, unless otherwise noted.

Subpart A—General Provisions

§ 514.1 Applications.

(a) Applications to be filed under section 512(b) of the act shall be submitted in the form described in paragraph (b) of this section. If any part of the application is in a foreign language, an accurate and complete English translation shall be appended to such part. Translations of literature printed in a foreign language shall be accompanied by copies of the original publication. The application must be signed by the applicant or by an authorized attorney, agent, or official. If the applicant or such authorized representative does not reside or have a place of business within the United States, the application must also furnish the name and post office address of, and must be countersigned by, an authorized attorney, agent, or official

residing or maintaining a place of business within the United States. Pertinent information may be incorporated in, and will be considered as part of, an application on the basis of specific reference to such information, including information submitted under the provisions of § 511.1 of this chapter, in the files of the Food and Drug Administration; however, the reference must be specific in identifying the information. Any reference to information furnished by a person other than the applicant may not be considered unless its use is authorized in a written statement signed by the person who submitted it.

(b) Applications for new animal drugs shall be submitted in triplicate and assembled in the manner prescribed by paragraph (b)(15) of this section, and shall include the following information:

(1) *Identification.* Whether the submission is an original or supplemental application; the name and the address of the applicant; the date of the application; the trade name(s) (if one has been proposed) and chemical name(s) of the new animal drug. Upon receipt, the application will be assigned a number NADA —, which shall be used for all correspondence with respect to the application.

(2) *Table of contents and summary.* The application shall be organized in a cohesive fashion, shall contain a table of contents which identifies the data and other material submitted, and shall contain a well-organized summary and evaluation of the data in the following form:

(i) *Chemistry:*

(a) Chemical structural formula or description for any new animal drug substance.

(b) Relationship to other chemically or pharmacologically related drugs.

(c) Description of dosage form and quantitative composition.

(ii) *Scientific rationale and purpose* the new animal drug is to serve:

(a) *Clinical purpose.*

(b) *Highlights of laboratory studies:* The reasons why certain types of studies were done or omitted as related to the proposed conditions of use and to information already known about this class of compounds. Emphasize any

unusual or particularly significant pharmacological effects or toxicological findings.

(c) *Highlights of clinical studies:* The rationale of the clinical study plan showing why types of studies were done, amended, or omitted as related to laboratory studies and prior clinical experience.

(d) *Conclusions:* A short statement of conclusions combining the major points of effectiveness and safety as they relate to the use of the new animal drug.

(3) *Labeling.* Three copies of each piece of all labeling to be used for the article (total of 9).

(i) All labeling should be identified to show its position on, or the manner in which it is to accompany the market package.

(ii) Labeling for nonprescription new animal drugs should include adequate directions for use by the layman under all conditions of use for which the new animal drug is intended, recommended, or suggested in any of the labeling or advertising sponsored by the applicant.

(iii) Labeling for prescription veterinary drugs should bear adequate information for use under which veterinarians can use the new animal drug safely and for the purposes for which it is intended, including those purposes for which it is to be advertised or represented, in accord with § 201.105 of this chapter.

(iv) All labeling for prescription or nonprescription new animal drugs shall be submitted with any necessary use restrictions prominently and conspicuously displayed.

(v) Labeling for new animal drugs intended for use in the manufacture of medicated feeds shall include:

(a) Specimens of labeling to be used for such new animal drug with adequate directions for the manufacture and use of finished feeds for all conditions for which the new animal drug is intended, recommended, or suggested in any of the labeling, including advertising, sponsored by the applicant. Ingredient labeling may utilize collective names as provided in § 501.110 of this chapter.

(b) Representative labeling proposed to be used for Type B and Type C

medicated feeds containing the new animal drug.

(vi) Draft labeling may be submitted for preliminary consideration of an application. Final printed labeling will ordinarily be required prior to approval of an application. Proposed advertising for veterinary prescription drugs may be submitted for comment or approval.

(4) *Components and composition.* A complete list of all articles used for production of the new animal drug including a full list of the composition of each article:

(i) A full list of the articles used as components of the new animal drug. This list should include all substances used in the synthesis, extraction, or other method of preparation of any new animal drug and in the preparation of the finished dosage form, regardless of whether they undergo chemical change or are removed in the process. Each component should be identified by its established name, if any, or complete chemical name, using structural formulas when necessary for specific identification. If any proprietary name is used, it should be followed by a complete quantitative statement of composition. Reasonable alternatives for any listed component may be specified.

(ii) A full statement of the composition of the new animal drug. The statement shall set forth the name and amount of each ingredient, whether active or not, contained in a stated quantity of the new animal drug in the form in which it is to be distributed (for example, amount per tablet or milliliter) and a batch formula representative of that to be employed for the manufacture of the finished dosage form. All components should be included in the batch formula regardless of whether they appear in the finished product. Any calculated excess of an ingredient over the label declaration should be designated as such and percent excess shown. Reasonable variation may be specified.

(iii) If it is a new animal drug produced by fermentation:

(a) Source and type of microorganism used to produce the new animal drug.

(b) Composition of media used to produce the new animal drug.

(c) Type of precursor used, if any, to guide or enhance production of the antibiotic during fermentation.

(d) Name and composition of preservative, if any, used in the broth.

(e) A complete description of the extraction and purification processes including the names and compositions of the solvents, precipitants, ion exchange resins, emulsifiers, and all other agents used.

(f) If the new animal drug is produced by a catalytic hydrogenation process (such as tetracycline from chlortetracycline), a complete description of each chemical reaction with graphic formulas used to produce the new animal drug, including the names of the catalyst used, how it is removed, and how the new animal drug is extracted and purified.

(5) *Manufacturing methods, facilities, and controls.* A full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of the new animal drug. This description should include full information with respect to any new animal drug in sufficient detail to permit evaluation of the adequacy of the described methods of manufacture, processing, and packing, and the described facilities and controls to determine and preserve the identity, strength, quality, and purity of the new animal drug, and the following:

(i) If the applicant does not himself perform all the manufacturing, processing, packaging, labeling, and control operations for any new animal drug, he shall: Identify each person who will perform any part of such operations and designate the part; and provide a signed statement from each such person fully describing, directly or by reference, the methods, facilities, and controls he will use in his part of the operation. The statement shall include a commitment that no changes will be made without prior approval by the Food and Drug Administration, unless permitted under § 514.8.

(ii) A description of the qualifications, including educational background and experience, of the techni-

cal and professional personnel who are responsible for assuring that the new animal drug has the identity, strength, quality, and purity it purports or is represented to possess, and a statement of their responsibilities.

(iii) A description of the physical facilities including building and equipment used in manufacturing, processing, packaging, labeling, storage, and control operations.

(iv) The methods used in the synthesis, extraction, isolation, or purification of any new animal drug. When the specifications and controls applied to such new animal drugs are inadequate in themselves to determine its identity, strength, quality, and purity, the methods should be described in sufficient detail, including quantities used, times, temperature, pH, solvents, etc., to determine these characteristics. Alternative methods or variations in methods within reasonable limits that do not affect such characteristics of the new animal drug may be specified. A flow sheet and indicated equations should be submitted when needed to explain the process.

(v) Precautions to insure proper identity, strength, quality, and purity of the raw materials, whether active or not, including:

(a) The specifications for acceptance and methods of testing for each lot of raw material.

(b) A statement as to whether or not each lot of raw materials is given a serial number to identify it, and the use made of such numbers in subsequent plant operations.

(vi) The instructions used in the manufacturing, processing, packaging, and labeling of each dosage form of the new animal drug, including:

(a) The method of preparation of the master formula records and individual batch records and the manner in which these records are used.

(b) The number of individuals checking weight or volume of each individual ingredient entering into each batch of the new animal drug.

(c) A statement as to whether or not the total weight or volume of each batch is determined at any stage of the manufacturing process subsequent to making up a batch according to the

formula card and, if so, at what stage and by whom it is done.

(d) The precautions used in checking the actual package yield produced from a batch of the new animal drug with the theoretical yield. This should include a description of the accounting for such items as discards, breakage, etc., and the criteria used in accepting or rejecting batches of drugs in the event of an unexplained discrepancy.

(e) The precautions used to assure that each lot of the new animal drug is packaged with the proper label and labeling, including provisions for labeling storage and inventory control.

(f) Any special precautions used in the operations.

(vii) The analytical controls used during the various stages of the manufacturing, processing, packaging, and labeling of the new animal drug, including a detailed description of the collection of samples and the analytical procedures to which they are subjected. The analytical procedures should be capable of determining the active components within a reasonable degree of accuracy and of assuring the identity of such components.

(a) A description of practicable methods of analysis of adequate sensitivity to determine the amount of the new animal drug in the final dosage form should be included. The dosage form may be a finished pharmaceutical product, a Type A medicated article, a Type B or a Type C medicated feed, or a product for use in animal drinking water. Where two or more active ingredients are included, methods should be quantitative and specific for each active ingredient.

(b) If the article is one that is represented to be sterile, the same information with regard to the manufacturing, processing, packaging, and the collection of samples of the drug should be given for sterility controls. Include the standards used for acceptance of each lot of the finished drug.

(viii) An explanation of the exact significance of any batch control numbers used in the manufacturing, processing, packaging, and labeling of the new animal drug, including such control numbers that may appear on the label of the finished article. State whether these numbers enable deter-

ination of the complete manufacturing history of the product. Describe any methods used to permit determination of the distribution of any batch its recall is required.

(ix) Adequate information with respect to the characteristics of and the test methods employed for the container, closure, or other component parts of the drug package to assure their suitability for the intended use.

(x) A complete description of, and data derived from, studies of the stability of the new animal drug in the final dosage form, including information showing the suitability of the analytical methods used. A description of any additional stability studies underway or planned. Stability data for the finished dosage form of the new animal drug in the container in which it is to be marketed, including any proposed multiple dose container, and, if it is to be put into solution at the time of dispensing, for the solution prepared as directed. If the new animal drug is intended for use in the manufacture of Type C medicated feed as defined in § 558.3 of this chapter, stability data derived from studies in which representative formulations of medicated feed articles are used. Similar data may be required for Type C medicated feeds as determined by the Food and Drug Administration on a case-by-case basis. Expiration dates will be proposed for finished pharmaceutical dosage forms and Type A medicated articles. If the data indicate that an expiration date is needed for Type B or Type C medicated feeds, the applicant shall propose such expiration date. If no expiration date is proposed for Type B or Type C medicated feeds, the applicant shall justify the absence with data.

(i) Additional procedures employed which are designed to prevent contamination and otherwise assure proper control of the product. An application may be refused unless it includes adequate information showing the methods used in, and the facilities and controls used for, the manufacturing, processing, and packaging of the new animal drug are adequate to preserve its identity, strength, quality and purity in conformity with good manufacturing practice and identifies

each establishment, showing the location of the plant conducting these operations.

(6) *Samples.* Samples of the new animal drug and articles used as components and information concerning them may be requested by the Bureau of Veterinary Medicine as follows:

(i) Each sample shall consist of four identical, separately packaged subdivisions, each containing at least three times the amount required to perform the laboratory test procedures described in the application to determine compliance with its control specifications for identity and assays. Each of the samples submitted shall be appropriately packaged and labeled to preserve its characteristics, to identify the material and the quantity in each subdivision of the sample, and to identify each subdivision with the name of the applicant and the new animal drug application to which it relates. Included are:

(a) A sample or samples of any reference standard and blank used in the procedures described in the application for assaying each new animal drug and other assayed components of the finished new animal drug.

(b) A representative sample or samples of each strength of the finished dosage form proposed in the application and employed in the clinical investigations and a representative sample or samples of each new animal drug from the batch(es) employed in the production of such dosage form.

(c) A representative sample or samples of finished market packages of each strength of the dosage form of the new animal drug prepared for initial marketing and, if any such sample is not from a representative commercial-scale production batch, such a sample from a representative commercial-scale production batch, and a representative sample or samples of each new animal drug from the batch(es) employed in the production of such dosage form, provided that in the case of new animal drugs marketed in large packages the sample should contain only three times a sufficient quantity of the new animal drug to allow for performing the control tests for drug identity and assays.

(ii) The following information shall be included for the samples when requested:

(a) For each sample submitted, full information regarding its identity and the origin of any new animal drug contained therein (including a statement whether it was produced on a laboratory, pilot-plant, or full-production scale) and detailed results of all laboratory tests made to determine the identity, strength, quality, and purity of the batch represented by the sample, including assays.

(b) For any reference standard submitted, a complete description of its preparation and the results of all laboratory tests on it. If the test methods used differed from those described in the application, full details of the methods employed in obtaining the reporting results.

(7) *Analytical methods for residues.* Applications shall include a description of practicable methods for determining the quantity, if any, of the new animal drug in or on food, and any substance formed in or on food because of its use, and the proposed tolerance or withdrawal period or other use restrictions to ensure that the proposed use of this drug will be safe. When data or other adequate information establish that it is not reasonable to expect the new animal drug to become a component of food at concentrations considered unsafe, a regulatory method is not required.

(i) The kind of information required by this subdivision may include: Complete experimental protocols for determining drug residue levels in the edible products, and the length of time required for residues to be eliminated from such products following the drug's use; residue studies conducted under appropriate (consistent with the proposed usage) conditions of dosage, time, and route of administration to show levels, if any, of the drug and/or its metabolites in test animals during and upon cessation of treatment and at intervals thereafter in order to establish a disappearance curve; if the drug is to be used in combination with other drugs, possible effects of interaction demonstrated by the appropriate disappearance curve or depletion patterns after drug with-

drawal under appropriate (consistent with the proposed usage) conditions of dosage, time, and route of administration; if the drug is given in the feed or water, appropriate consumption records of the medicated feed or water and appropriate performance data in the treated animal; if the drug is to be used in more than one species, drug residue studies or appropriate metabolic studies conducted for each species that is food-producing. To provide these data, a sufficient number of birds or animals should be used at each sample interval. Appropriate use of labeled compounds (e.g. radioactive tracers), may be utilized to establish metabolism and depletion curves. Drug residue levels ordinarily should be determined in muscle, liver, kidney, and fat and where applicable, in skin, milk, and eggs (yolk and egg white). As a part of the metabolic studies, levels of the drug or metabolite should be determined in blood where feasible. Samples may be combined where necessary. Where residues are suspected or known to be present in litter from treated animals, it may be necessary to include data with respect to such residues becoming components of other agricultural commodities because of use of litter from treated animals.

(ii) A new animal drug that has the potential to contaminate human food with residues whose consumption could present a risk of cancer to people must satisfy the requirements of Subpart E of Part 500 of this chapter.

(8) *Evidence to establish safety and effectiveness.* (i) An application may be refused unless it contains full reports of adequate tests by all methods reasonably applicable to show whether or not the new animal drug is safe and effective for use as suggested in the proposed labeling.

(ii) An application may be refused unless it includes substantial evidence, consisting of adequate and well-controlled investigations, including field investigation, by experts qualified by scientific training and experience to evaluate the effectiveness of the new animal drug involved, on the basis of which it could fairly and reasonably be concluded by such experts that the new animal drug will have the effect it

purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling.

(iii) An application may be refused unless it contains detailed reports of the investigations, including studies made on laboratory animals, in which the purpose, methods, and results obtained are clearly set forth of acute, subacute, and chronic toxicity, and unless it contains appropriate clinical laboratory results related to safety and efficacy. Such information should include identification of the person who conducted each investigation, a statement of where the investigations were conducted, and where the raw data are available in the application.

(iv) All information pertinent to an evaluation of the safety and effectiveness of the new animal drug received or otherwise obtained by the applicant from any source, including information derived from other investigations or commercial marketing (for example, outside the United States), or reports in the scientific literature, both favorable and unfavorable, involving the new animal drug that is the subject of the application and related new animal drugs shall be submitted. An adequate summary may be acceptable in lieu of a reprint of a published report that only supports other data submitted. Include any evaluation of the safety or effectiveness of the new animal drug that has been made by the applicant's veterinary or medical department, expert committee, or consultants.

(v) If the new animal drug is a combination of previously investigated or marketed new animal drugs, an adequate summary of preexisting information from preclinical and clinical investigation and experience with its components, including all reports received or otherwise obtained by the applicant suggesting side effects, contraindications, and ineffectiveness in use of such components, shall be submitted. Such summary should include an adequate bibliography of publications about the components and may incorporate by reference information concerning such components previously submitted to the Food and Drug Administration by the applicant; with

written authorization, information may also be incorporated from the material that another applicant has on file with the Food and Drug Administration. Each ingredient designated as active in any new animal drug combination must make a contribution to the effect in the manner claimed or suggested in the labeling, and, if in the absence of express labeling claims of advantages for the combination such a product purports to be better than either component alone, it must be established that the new animal drug has that purported effectiveness.

(vi) An application shall include a complete list of the names and post office addresses of all investigators who received the new animal drug. This may be incorporated in whole or in part by reference to information submitted under the provisions of § 511.1 of this chapter.

(vii) Explain any omission of reports from any investigator to whom the investigational new animal drug has been made available. The unexplained omission of any reports of investigations made with the new animal drug by the applicant or submitted to him by an investigator or the unexplained omission of any pertinent reports of investigations or clinical experience received or otherwise obtained by the applicant from published literature or other sources that would bias an evaluation of the safety of the new animal drug or its effectiveness in use, constitutes grounds for the refusal or withdrawal of the approval of an application.

(viii) If a sponsor has transferred any obligations for the conduct of any clinical study to a contract research organization, the application is required to include a statement containing the name and address of the contract research organization, identifying the clinical study, and listing the obligations transferred. If all obligations governing the conduct of the study have been transferred, a general statement of this transfer—in lieu of a listing of the specific obligations transferred—may be submitted.

(ix) If original subject records were audited or reviewed by the sponsor in the course of monitoring any clinical study to verify the accuracy of the

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case reports submitted to the sponsor, a list identifying each clinical study so audited or reviewed.

(9) *New animal drugs subject to section 512(n) of the act.* If the application is for a new animal drug subject to the certification provisions of section 512(n) of the act and the drug is included in regulations promulgated under section 507 of the act, the applicant may be exempted from the submission of some of the information required by paragraph (b)(8) of this section if the application includes data adequate to prove that the new animal drug is comparable to the new animal drug for which certification has been previously provided.

(10) *Supplemental applications.* If it is a supplemental application, full information shall be submitted on each proposed change concerning any statement made in the approved application.

(11) *Applicant's commitment.* It is understood that the labeling and advertising for the new animal drug will prescribe, recommend, or suggest its use only under the conditions stated in the labeling which is part of this application and if the article is a prescription new animal drug, it is understood that any labeling which furnishes or purports to furnish information for use or which prescribes, recommends, or suggests a dosage for use of the new animal drug will also contain, in the same language and emphasis, information for its use including indications, effects, dosages, routes, methods, and frequency and duration of administration, any relevant hazards, contraindications, side effects, and precautions contained in the labeling which is part of this application. It is understood that all representations in this application apply to the drug produced until changes are made in conformity with § 514.8.

(12) *Additional commitments.* (i) New animal drugs as defined in § 510.3 of this chapter, intended for use in the manufacture of animal feeds in any State will be shipped only to persons who may receive such drugs in accordance with § 510.7 of this chapter.

(ii) The methods, facilities, and controls described under item 5 of this application conform to the current good

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manufacturing practice regulations in Subchapter C of this chapter.

(iii) With respect to each nonclinical laboratory study contained in the application, either a statement that the study was conducted in compliance with the good laboratory practice regulations set forth in Part 58 of this chapter, or, if the study was not conducted in compliance with such regulations, a brief statement of the reason for the noncompliance.

(13) [Reserved]

(14) *Environmental assessment.* The applicant is required to submit either a claim for categorical exclusion under § 25.24 of this chapter or an environmental assessment under § 25.31 of this chapter.

(15) *Assembling and binding the application.* Assemble and bind an original and two copies of the application as follows:

(i) Bind the original or ribbon copy of the application as copy No. 1.

(ii) Bind two identical copies as copy No. 2 and copy No. 3.

(iii) Identify each front cover with the name of the applicant, new animal drug, and the copy number.

(iv) Number each page of the application sequentially in the upper right hand corner or in another location so that the page numbers remain legible after the application has been bound, and organize the application consistent with paragraphs (b) (1) through (14) of this section. Each copy should bear the same page numbering, whether sequential in each volume or continuous and sequential throughout the application.

(v) Include complete labeling in each of the copies. It is suggested that labeling be identified by date of printing or date of preparation.

(vi) Submit separate applications for each different dosage form of the drug proposed. Repeating basic information pertinent to all dosage forms in each application is unnecessary if reference is made to the application containing such information. Include in each application information applicable to the specific dosage form, such as labeling, composition, stability data, and method of manufacture.

(vii) Submit in folders amendments, supplements, and other correspond-

ence sent after submission of an original application. The front cover of these submissions should be identified with the name of the applicant, new animal drug, copy number, and the new animal drug application number, if known.

(c) When a new animal drug application is submitted for a new animal drug which has a stimulant, depressant, or hallucinogenic effect on the central nervous system, if it appears that the drug has a potential for abuse, the Commissioner shall forward that information to the Attorney General of the United States.

(d) *Minor use applications.* Applications for minor use new animal drugs:

(1) *Definitions.* For the purpose of this section:

(i) "Minor use" means the use of: (a) new animal drugs in minor animal species, or (b) new animal drugs in any animal species for the control of a disease that (1) occurs infrequently or (2) occurs in limited geographic areas.

(ii) "Minor species" means animals other than cattle, horses, swine, chickens, turkeys, dogs, and cats. Sheep are minor species with respect to effectiveness and animal safety data collection requirements; sheep are a major species with respect to human safety data collection requirements arising from the possible presence of drug residues in food.

(2) *Animal safety, effectiveness, human food safety, and environmental considerations.* Guidelines for the preparation and submission of data to satisfy the requirements of section 512 of the act regarding animal safety, effectiveness, human food safety, and environmental considerations for new animal drugs intended for a "minor" (as defined in paragraph (d)(1)(i) of this section) are available from the Information and Education Resources Management Staff (HFV-13), Bureau of Veterinary Medicine, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

(3) *Animal safety and effectiveness.* Where the guidelines do not specifically provide for a particular "minor" use, the Bureau of Veterinary Medicine, upon request, will advise interested persons on the effectiveness and animal safety data regarding the

minor use that will be needed to satisfy the requirements of section 512 of the act. Where scientifically appropriate, the Bureau of Veterinary Medicine will allow the use of animal models and the extrapolation of data from a major species to a minor species to satisfy the requirements of the act.

(ii) *Human food safety and environmental considerations.* These guidelines do not specifically provide for a particular "minor use." Therefore, the Bureau of Veterinary Medicine will, upon request, advise interested persons of the data that will be needed. Where scientifically appropriate, the Bureau of Veterinary Medicine will allow the extrapolation of data from a major species to a minor species to satisfy the requirements of the act.

(Information collection requirements approved by the Office of Management and Budget under control number 0910-0032)

(Secs. 406, 408, 409, 501, 502, 503, 505, 506, 507, 510, 512-516, 518-520, 601, 701, 706, and 801, 52 Stat. 1049-1053 as amended, 1055, 1056 as amended, 1058 as amended, 55 Stat. 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511-517 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 399-407 as amended, 76 Stat. 794 as amended, 82 Stat. 343-351, 90 Stat. 539-574 (21 U.S.C. 346, 346a, 348, 351, 352, 353, 355, 356, 357, 360, 360b-360f, 360h-360i, 371, 376); secs. 215, 301, 351, 354-360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 241, 262, 243b-263n); secs. 512, 701(a), 52 Stat. 1055, 82 Stat. 343-351 (21 U.S.C. 360b, 371(a)))

[40 FR 13825, Mar. 27, 1975, as amended at 40 FR 52609, Nov. 11, 1975; 42 FR 15675, Mar. 22, 1977; 43 FR 60023, Dec. 22, 1978; 48 FR 1928, Jan. 14, 1983; 50 FR 7517, Feb. 22, 1985; 50 FR 14212, Apr. 11, 1985; 50 FR 16668, Apr. 26, 1985; 51 FR 7391, Mar. 3, 1986; 52 FR 8847, Mar. 19, 1987; 52 FR 49588, Dec. 31, 1987]

§ 514.2 Applications for animal feeds bearing or containing new animal drugs.

(a) Applications (Form FDA 1900) to be filed under section 512(m) of the act shall be completed, signed, and submitted in triplicate in the form described in paragraphs (b) and (c) of this section.

(b) Each application for a Type B or Type C medicated feed, as defined in

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§ 558.3 of this chapter, shall include the following information:

(1) The name and address of the applicant.

(2) The registration number assigned pursuant to section 510 of the act and last date of registration of each mill.

(3) Whether the submission is an original or supplemental application.

(4) Identification of the Type A medicated article, as defined in § 558.3 of this chapter, used by generic name, potency, and manufacturer.

(5) The species of animal(s) for which the feed is intended.

(6) The form of feed to be produced, i.e., mash, meal crumbles, pellets, liquid, or other specified form.

(7) Whether the feed is a Type B or Type C medicated feed.

(8) Whether the feed is for sale or for own use (not for sale).

(9) Level of the drug(s) in the finished feed, and the amount of Type A medicated article per ton contained therein.

(10) Identification of the regulation(s) in Subchapter E of this chapter on which approval relies.

(11) Labeling representative of each intended use as stated in the claim. Each generic label shall include the claim, drug level, mixing directions, feeding directions, caution and/or warning statements, and any other special directions required by the published regulation. This shall consist of bag labels, invoice copy, bulk labels, and placards when applicable.

(12) A commitment to establish and maintain a program of sampling and analysis consisting of an assay of the first batch manufactured, followed thereafter by two samples at periodic intervals during the calendar year. If a medicated feed contains a combination of drugs, only one of the drugs need be subject to analysis each time, provided the one tested is different from the one(s) previously tested. Reports of assays shall be kept on the premises for not less than 1 year after the date of manufacture of the medicated feed.

(13) A statement of the minimum and maximum assay value permitted from the labeled amount of the drug.

(14) Identification of the agent authorized to act on behalf of the applicant.

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(15) The applicant's name, responsible individual's title and original signature, and date.

(c) Upon approval, one copy of the application will be signed by an authorized employee of the Food and Drug Administration designated by the Commissioner, and it will be returned to the applicant.

(Information collection requirements approved by the Office of Management and Budget under control number 0910-0011)

(51 FR 7391, Mar. 3, 1986)

§ 514.6 Amended applications.

The applicant may submit an amendment to an application that is pending, including changes that may alter the conditions of use, the labeling, safety, effectiveness, identity, strength, quality, or purity of the drug or the adequacy of the manufacturing methods, facilities, and controls to preserve them, in which case the unamended application may be considered as withdrawn and the amended application may be considered resubmitted on the date on which the amendment is received by the Food and Drug Administration. The applicant will be notified of such date.

§ 514.7 Withdrawal of applications without prejudice.

The sponsor may withdraw his pending application from consideration as a new animal drug application upon written notification to the Food and Drug Administration. Such withdrawal may be made without prejudice to a future filing. Upon resubmission, the time limitation will begin to run from the date the resubmission is received by the Food and Drug Administration. The original application will be retained by the Food and Drug Administration although it is considered withdrawn. The applicant shall be furnished a copy at cost on request.

§ 514.8 Supplemental new animal drug applications.

(a)(1) After a new animal drug application is approved, a supplemental new animal drug application may propose changes. A supplemental application may omit statements made in the approved application concerning

which no change is proposed. Each supplemental application shall include up-to-date reports of any of the kinds of information required by § 510.300(a) of this chapter that has not previously been submitted. A supplemental application shall be accompanied by either a claim for categorical exclusion under § 25.24 of this chapter or an environmental assessment under § 25.31 of this chapter.

(2) A supplemental new animal drug application shall be submitted for any change beyond the variations provided for in the application, including changes in the scale of production such as from pilot-plant to production batch, that may alter the conditions of use, the labeling, safety, effectiveness, identity, strength, quality, or purity of the new animal drug, or the adequacy of the manufacturing methods, facilities, or controls to preserve them.

(3) If it is a prescription drug, any mailing or promotional piece used after the drug is placed on the market is labeling requiring a supplemental application, unless:

(i) The parts of the labeling furnishing directions, warnings, and information for use of the drug are the same in language and emphasis as labeling approved or permitted; and

(ii) Any other parts of the labeling are consistent with and not contrary to such approved or permitted labeling.

(4) The supplemental application shall be submitted as follows. A communication proposing a change in a new animal drug application should provide for any one of the following kinds of changes:

(i) Revision in labeling, such as updating information pertaining to effects, dosages, and side effects and contraindications, which includes information headed "side effects," "warnings," "precautions," and "contraindications."

(ii) Addition of claim.

(iii) Revision in manufacturing or control procedures; for example, changes in components, composition, method of manufacture, analytical control procedures, package or tablet size, etc.

(iv) Change in manufacturing facilities.

(v) Provision for outside firm to participate in the preparation, distribution, or packaging of a new animal drug (new distributor, packer, supplier, manufacturer, etc.); one firm per submission.

Any number of changes may be submitted at any one time; but if they fall into different categories as listed in paragraphs (a)(4) (i) through (v) of this section, the proposed changes should be covered by separate communications. Where, however, a change necessitates an overlap in categories, it should be submitted in a single communication. For example, a change in tablet potency would require other changes such as in components, composition, and labeling and should be submitted in a single communication.

(5) The following kinds of changes may be placed into effect without the approval of a supplemental application, if such change is fully described in the next periodic report required under § 510.300(b)(4) of this chapter or, when such a report is not required, in a written communication to the Food and Drug Administration within 60 days of the effective date of the change (this does not apply to a change proposed because of any mixup or any bacteriological or significant chemical, physical, or other change or deterioration in the drug or any failure of one or more distributed batches of the drug to meet its specifications):

(i) A different container size for solid oral dosage forms where container and closure are of the same materials as those provided for in the approved application.

(ii) Change in personnel not involving new facilities.

(iii) Change in equipment that does not alter the method of manufacture of a new animal drug.

(iv) Change from one commercial batch size to another without any change in manufacturing procedure.

(v) Change to more stringent specification without altering the method described in the approved application.

(vi) Inclusion of additional specifications and methods without deletion of those described in the approved application.

(vii) Alteration of specifications or methods for inactive ingredients to bring them into compliance with new or revised specifications or methods in an official compendium.

(viii) Initiation of a product identification coding system.

(ix) Addition to labeling of a reasonable expiration date where none was previously used, with related conditions of drug storage when appropriate, except when evidence shows that a significant deterioration of the drug under marketing conditions has occurred which necessitates the immediate submission of a report under § 510.300(b)(1) of this chapter. The report or written communication describing such change in labeling should include stability data justifying the expiration date and recommended conditions of storage.

(x) Change from paper labels to direct printing on glass or other kinds of immediate containers without a change in text.

(6) Approval of a supplemental new animal drug application will not be required to provide for an additional distributor to distribute a drug which is the subject of an approved new animal drug application if the conditions described below are met prior to putting such a change into effect. An order may issue refusing approval if any condition is not met or if any of the reasons for refusing or withdrawing approval, as stated in section 512(d) and (e) of the act or § 514.110 applies. For the purposes of maintaining records and making reports under the requirements of § 510.300 of this chapter, a distributor provided for under this section shall be considered an "applicant" within the meaning of § 510.300(b) of this chapter. Said conditions are:

(i) A supplemental application is furnished to the Food and Drug Administration to provide for a designated distributor.

(ii) There are no changes from the conditions of the approved application except for a different and suitable proprietary name of the new animal drug (if one is used) and the name and address of the distributor as used on the label and labeling. The name of the distributor shall be accompanied by an

appropriate qualifying phrase such as "manufactured for" or "distributed by."

(iii) A distributor's statement is furnished to the Food and Drug Administration identifying the category of his operations (for example, wholesaler, retailer) and stating: That he will distribute the new animal drug only under the labeling provided for in the new animal drug application; that any other labeling or advertising for the drug will prescribe, recommend, or suggest its use only under the conditions stated in the labeling provided for in the application; and, if the drug is a prescription article, that he is regularly and lawfully engaged in the distribution or dispensing of prescription drugs.

(iv) Nine copies of the printed labels and other labeling to be used by the distributor are submitted, identified with the new animal drug application number.

(b) When necessary for the safety or effectiveness of the drug, a supplemental new animal drug application shall specify a period of time within which the proposed change will be made.

(c) If a material change is made in the components' composition, manufacturing methods, facilities, or controls, or in the labeling or advertising, from the representations in an approved application for a new animal drug (except changes conforming to the conditions set forth in paragraph (a)(5) and (6) and/or paragraphs (d), (e), (f), and (g) of this section), and the drug is marketed before a supplement is approved for such change, approval of the application may be suspended or withdrawn as provided in section 512(e) of the act.

(d) Changes of the following kinds proposed in supplemental new animal drug applications should be placed into effect at the earliest possible time:

(1) The addition to package labeling, promotional labeling, and prescription drug advertising of additional warning, contraindication, side effect, and precaution information.

(2) The deletion from package labeling, promotional labeling, and drug advertising of false, misleading, or un-

supported indications for use or claims for effectiveness.

(3) Changes in the methods, facilities, or controls used for the manufacture, processing, packing, or holding of the new animal drug (other than utilization of establishments not covered by the approval that is in effect) that give increased assurance that the drug will have the characteristics of identity, strength, quality, and purity which it purports or is represented to possess.

(e) The Food and Drug Administration will take no action against a new animal drug or applicant solely because changes of the kinds described in paragraph (d) of this section are placed into effect by the applicant prior to his receipt of a written notice of approval of the supplemental new animal drug application if all the following conditions are met:

(1) The supplemental new animal drug application providing a full explanation of the basis for the changes has been submitted, plainly marked on the mailing cover and on the supplement, "Special new animal drug application Supplement—changes being effected."

(2) The applicant specifically informs the Food and Drug Administration of the date on which such changes are being effected and submits to the Administration nine printed copies of any revised labeling to be placed in use, identified with the new animal drug application number.

(3) All promotional labeling and all drug advertising are promptly revised consistent with the changes made in the labeling on or within the new animal drug package.

(f) When a supplemental new animal drug application proposes changes only of the kinds described in paragraph (d) of this section, and the applicant informs the Food and Drug Administration that the changes are being put into effect, such notification will be regarded as an agreement by the applicant to an extension of the time for formal action on the application.

(g) In addition to changes as permitted by paragraphs (d) and (e) of this section, an applicant may place into effect changes proposed in a supplement

ment to a new animal drug application that became effective prior to October 10, 1962, upon written notification from the Food and Drug Administration that such action is permitted, without approval of the supplemental application, pending the completion of the review of the effectiveness of such drug by the National Academy of Sciences-National Research Council and a determination as to whether there are grounds for refusing approval under section 512(d) of the act or for invoking section 512(e) of the act. The Food and Drug Administration will take no action against a new animal drug or an applicant solely because changes that have been permitted in a written communication are placed into effect by the applicant prior to his receipt of a written notice of approval of the supplemental new animal drug application.

(h) Except as provided in paragraphs (e) and (g) of this section, no provision of this section shall limit the authority of the Secretary or of the Commissioner to suspend or withdraw approval of a new animal drug application in accord with the provisions of section 512(e) of the act or to initiate any other regulatory proceedings with respect to a drug or applicant under provisions of the act.

(i) Changes from the conditions of an approved new animal drug application in accord with the provisions of paragraphs (d), (e), and (g) of this section are permitted on the basis of a temporary deferral of final action on the supplemental application under the provisions of section 512 (c), (d), or (e) of the act.

(j) When an applicant receives written notification from the Food and Drug Administration, under the provisions of paragraph (g) of this section, that he may place into effect changes proposed in a supplemental application without approval of the supplemental application, he may within 30 days submit a written request that the Food and Drug Administration process the supplemental application. In such case, the change shall not be put into effect until approved. Within 180 days of the receipt of such written request, the Food and Drug Administration will approve the supplemental applica-

tion or furnish notice of an opportunity for a hearing under the provisions of section 512 (d) or (e), or both, of the act on a proposal to refuse approval of the supplemental application or to withdraw approval of the application and supplements thereto.

(k) A supplement to an application that became effective prior to October 10, 1962, may include a written statement to the effect that a temporary deferral of final action under the provisions of paragraph (d), (e), or (g) of this section is unacceptable to the applicant and that the applicant requests action as provided in section 512(c) of the act. Final action on such supplemental applications will be expedited in accord with applicable provisions of section 512 of the act and regulations in this Subchapter E. In such cases, if the applicant places into effect any of the proposed changes prior to his receipt of a written notice of approval of the supplemental new animal drug application, such action may be regarded by the Food and Drug Administration as a basis for invoking the provisions of section 512(e) (1)(D) of the act; that is, the applicant may be furnished notice of an opportunity for a hearing on a proposal to withdraw approval of the application on the ground that the application contains an untrue statement of a material fact related to the changes from the conditions approved in the application.

(l) A supplemental application that contains nonclinical laboratory studies shall include, with respect to each nonclinical study, either a statement that the study was conducted in compliance with the requirements set forth in Part 58 of this chapter, or, if the study was not conducted in compliance with such regulations, a brief statement of the reason for the non-compliance.

(Secs. 406, 408, 409, 501, 502, 503, 505, 506, 507, 510, 512-516, 518-520, 601, 701, 706, and 801, 52 Stat. 1049-1053 as amended, 1055, 1056 as amended, 1058 as amended, 55 Stat. 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511-517 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 399-407 as amended, 76 Stat. 794 as amended, 82 Stat. 343-351, 90 Stat. 539-574 (21 U.S.C. 346, 346a, 348, 351, 352, 353, 355, 356, 357, 360, 360b-360f, 360h-360i, 371, 376); secs. 215, 301, 351,

354-360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 241, 262, 263b-263n))

[40 FR 13825, Mar. 27, 1975, as amended at 50 FR 7517, Feb. 22, 1985; 50 FR 16668, Apr. 26, 1985]

§ 514.9 Supplemental applications for animal feeds bearing or containing new animal drugs.

(a) After an application for an animal feed bearing or containing a new animal drug has been approved, a supplemental application may propose changes.

(b) A supplemental application shall be submitted for any change which deviates from the conditions under which the application was originally approved.

(c) Each supplemental application shall be accompanied by a fully completed Form FDA 1900 in triplicate including an explanation of the changes proposed.

[40 FR 13825, Nov. 27, 1975, as amended at 42 FR 15675, Mar. 22, 1977; 50 FR 16668, Apr. 26, 1985; 51 FR 7391, Mar. 3, 1986]

§ 514.10 Confidentiality of data and information in an investigational new animal drug notice and a new animal drug application; file for an antibiotic drug.

(a) The rules established in §§ 514.12 and 514.11 of this chapter with regard to the confidentiality of an investigational new animal drug notice and a new animal drug application file shall apply to such notices and files for antibiotic drugs for new animal drug use.

(b) All records showing the Food and Drug Administration's testing of and action on a particular lot of a certifiable antibiotic drug for veterinary use are immediately available for public disclosure.

§ 514.11 Confidentiality of data and information in a new animal drug application file.

(a) For purposes of this section the "NADA file" includes all data and information submitted with or incorporated by reference in the NADA. INAD's incorporated into the NADA, supplemental NADA's, reports under §§ 510.300 and 510.301 of this chapter,

master files, and other related submissions. The availability for public disclosure of any record in the NADA file shall be handled in accordance with the provisions of this section.

(b) The existence of an NADA file will not be disclosed by the Food and Drug Administration before an approval has been published in the FEDERAL REGISTER, unless it has previously been publicly disclosed or acknowledged.

(c) If the existence of an NADA file has not been publicly disclosed or acknowledged, no data or information in the NADA file is available for public disclosure.

(d) If the existence of an NADA file has been publicly disclosed or acknowledged before an approval has been published in the FEDERAL REGISTER, no data or information contained in the file is available for public disclosure before such approval is published, but the Commissioner may, in his discretion, disclose a summary of such selected portions of the safety and effectiveness data as are appropriate for public consideration of a specific pending issue, e.g., at an open session of a Food and Drug Administration advisory committee or pursuant to an exchange of important regulatory information with a foreign government.

(e) After an approval has been published in the FEDERAL REGISTER, the following data and information in the NADA file are immediately available for public disclosure unless extraordinary circumstances are shown:

(1) All safety and effectiveness data and information previously disclosed to the public, as defined in § 20.81 of this chapter.

(2) A summary or summaries of the safety and effectiveness data and information submitted with or incorporated by reference in the NADA file. Such summaries do not constitute the full reports of investigations under section 512(b)(1) of the act (21 U.S.C. 360b(b)(1)) on which the safety or effectiveness of the drug may be approved. Such summaries shall consist of the following: (i) For an NADA approved prior to July 1, 1975, internal agency records that describe such data and information, e.g., a summary of basis for approval or internal reviews

of the data and information, after deletion of:

(a) Names and any information that would identify the investigators.

(b) Any inappropriate gratuitous comments unnecessary to an objective analysis of the data and information.

(ii) For an NADA approved on or after July 1, 1975, a summary of such data and information prepared in one of the following two alternative ways shall be publicly released when the approval is published in the FEDERAL REGISTER.

(a) The Bureau of Veterinary Medicine may at an appropriate time prior to approval of the NADA require the applicant to prepare a summary of such data and information, which will be reviewed and, where appropriate, revised by the Bureau.

(b) The Bureau of Veterinary Medicine may prepare its own summary of such data and information.

(3) A protocol for a test or study, unless it is shown to fall within the exemption established for trade secrets and confidential commercial information in § 20.61 of this chapter.

(4) Adverse reaction reports, product experience reports, consumer complaints, and other similar data and information, after deletion of:

(i) Names and any information that would identify the person using the product.

(ii) Names and any information that would identify any third party involved with the report, such as a physician, hospital, or other institution.

(5) A list of all active ingredients and any inactive ingredients previously disclosed to the public as defined in § 20.81 of this chapter.

(6) An assay method or other analytical method, unless it serves no regulatory or compliance purpose and is shown to fall within the exemption established in § 20.61 of this chapter.

(7) All correspondence and written summaries of oral discussions relating to the NADA, in accordance with the provisions of Part 20 of this chapter.

(f) All safety and effectiveness data and information not previously disclosed to the public are available for public disclosure at the time any one of the following events occurs unless

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extraordinary circumstances are known:

(1) The NADA has been abandoned and no further work is being undertaken with respect to it.

(2) A final determination is made that the NADA is not approvable, and all legal appeals have been exhausted.

(3) Approval of the NADA is withdrawn, and all legal appeals have been exhausted.

(4) A final determination has been made that the animal drug is not a new animal drug.

(5) A final determination has been made that the animal drug may be marketed without submission of such safety and/or effectiveness data and information.

(g) The following data and information in an NADA file are not available for public disclosure unless they have been previously disclosed to the public as defined in § 20.81 of this chapter or they relate to a product or ingredient that has been abandoned and they no longer represent a trade secret or confidential commercial or financial information as defined in § 20.61 of this chapter:

(1) Manufacturing methods or processes, including quality control procedures.

(2) Production, sales, distribution, and similar data and information, except that any compilation of such data and information aggregated and prepared in a way that does not reveal data or information which is not available for public disclosure under this provision is available for public disclosure.

(3) Quantitative or semiquantitative formulas.

(h) For purposes of this regulation, safety and effectiveness data include all studies and tests of an animal drug on animals and all studies and tests on the animal drug for identity, stability, purity, potency, and bioavailability.

(Sec. 201 et seq., Pub. L. 717, 52 Stat. 1040 et seq., as amended (21 U.S.C. 321 et seq.); as amended (42 U.S.C. 201 et seq.); Pub. L. sec. 1 et seq., Pub. L. 410, 58 Stat. 632 et seq., 90-23, 81 Stat. 54-56, as amended by 88 Stat. 1561-1565 (5 U.S.C. 552))

[40 FR 13825, Mar. 27, 1975, as amended at 42 FR 3109, Jan. 14, 1977; 42 FR 15675, Mar. 22, 1977]

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§ 514.12 Confidentiality of data and information in an investigational new animal drug notice.

(a) The existence of an INAD notice will not be disclosed by the Food and Drug Administration unless it has previously been publicly disclosed or acknowledged.

(b) The availability for public disclosure of all data and information in an INAD file shall be handled in accordance with provisions established in § 514.11.

§ 514.15 Untrue statements in applications.

Among the reasons why an application for a new animal drug or animal feed bearing or containing a new animal drug may contain an untrue statement of a material fact are:

(a) Differences in:

(1) Conditions of use prescribed, recommended, or suggested by the applicant for the product from the conditions of such use stated in the application;

(2) Articles used as components of the product from those listed in the application;

(3) Composition of the product from that stated in the application;

(4) Methods used in or the facilities and controls used for the manufacture, processing, or packing of the product from such methods, facilities, and controls described in the application;

(5) Labeling from the specimens contained in the application; or

(b) The unexplained omission in whole or in part from an application or from an amendment or supplement to an application or from any record or report required under the provisions of section 512 of the act and § 510.300 or § 510.301 of this chapter of any information obtained from:

(1) Investigations as to the safety, effectiveness, identity, strength, quality, or purity of the drug, made by the applicant on the drug, or

(2) Investigations or experience with the product that is the subject of the application, or any related product, available to the applicant from any source if such information is pertinent to an evaluation of the safety, effec-

tiveness, identity, strength, quality, or purity of the drug, when such omission would bias an evaluation of the safety or effectiveness of the product.

(c) Any nonclinical laboratory study contained in the application was not conducted in compliance with the good laboratory practice regulations as set forth in Part 58 of this chapter, and the application fails to include a brief statement of the reason for the noncompliance.

(Secs. 406, 408, 409, 501, 502, 503, 505, 506, 507, 510, 512-516, 518-520, 601, 701, 706, and 801, 52 Stat. 1049-1053 as amended, 1055, 1056 as amended, 1058 as amended, 55 Stat. 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511-517 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 399-407 as amended, 76 Stat. 794 as amended, 82 Stat. 343-351, 90 Stat. 539-574 (21 U.S.C. 346, 346a, 348, 351, 352, 353, 355, 356, 357, 360, 360b-360f, 360h-360i, 371, 376); secs. 215, 301, 351, 354-360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 241, 262, 263b-263n))

[40 FR 13825, Mar. 27, 1975, as amended at 49 FR 7226, Feb. 28, 1984; 50 FR 7517, Feb. 22, 1985]

§ 514.50 Requests for certification, check tests and assays, and working standards for animal drugs subject to section 512(n) of the act; information and samples required.

(a) A request for certification of a batch (antibiotic Form 7/Form FDA-1677) is to be addressed to the Food and Drug Administration, National Center for Antibiotic Analysis (HFD-430), 200 C St. SW., Washington, DC 20204.

(b)(1) The initial request for certification of a batch of any drug submitted by any person shall be preceded or accompanied by a full statement of the facilities and controls used to maintain the identity, strength, quality, and purity of each batch of such drug, including descriptions of:

(i) The methods and processes used in the manufacture of the drug;

(ii) The tests and assays of the drug made during the manufacture of the batch and after it is packaged; and

(iii) The laboratory facilities used in such controls.

(2) Such initial request shall also be preceded or accompanied by the key of the batch marks used by such

person and by specimens of all labeling to be used for such drug.

(c) A person who requests certification or check tests and assays of a batch shall submit with his request the following information and samples:

(1) The batch mark of the drug.

(2) The quantity of each ingredient used in making the batch and a statement that each such ingredient conforms to the requirements or standards prescribed therefor, if any, by specific regulations or official compendium or otherwise approved by the Commissioner.

(3) The size of the batch, including the number of containers of each size in the batch.

(4) The date of the latest assay of the batch.

(5) The results of the latest tests and assays made by or for him on the batch as required for the drug by specific regulations.

(6) The batch mark(s) of the antibiotic(s) used in making the batch.

(7) Unless previously submitted, the results and dates of the latest tests and assays made by or for him on the antibiotic(s) used in making the batch as required by specific regulations.

(8) The number of accurately representative samples that are required for the batch by specific regulations.

(i) In the case of drugs such as dry powders, solutions, ointments, and suspensions, the sample shall be collected by taking single immediate containers, before or after labeling, at such intervals throughout the entire time of packaging the batch that the quantities packaged during the intervals are approximately equal. In no case, however, shall more than 5,000 immediate containers have been packaged during each such interval of sampling, except for a sample collected for sterility testing.

(ii) In the case of drugs in unit dosage forms, such as tablets, capsules, or suppositories, samples shall be collected as follows:

(a) From batches exceeding 500,000 units, a representative sample consisting of 100 units shall be collected by taking single units at approximately equal intervals throughout the final production of the batch. If the person

packaging the units into dispensing-size containers is not the manufacturer, a representative sample consisting of 100 units shall be collected by taking single units at approximately equal intervals during packaging.

(b) From batches of 500,000 units or less, a representative sample consisting of not more than 100 units shall be collected by taking single units at approximately equal intervals throughout the final production of the batch. If the person packaging the units into dispensing-size containers is not the manufacturer, the samples shall be collected by taking single units at approximately equal intervals during packaging. In no case shall more than 5,000 units be produced or packaged during a sampling interval. The minimum acceptable sample size shall be as specified in the appropriate monograph.

(c) When the manufacturing process is such that it is not feasible to collect the samples throughout the final production of the batch (e.g., if tablets are subjected to further processing, such as polishing or coating, after being compressed), the samples may be collected from bulk containers of the finished product, according to the following requirements:

(1) For batches exceeding 500,000 units: If the batch is in more than 100 containers, the sample is one unit from each container. If the batch is in 100 containers or less, the sample is 100 units, taken in approximately equal amounts from each container.

(2) For batches of 500,000 units or less: If the batch is in more than 100 containers, the sample is 1 unit from each container. If the batch is in 100 containers or less, the sample is at least 1 unit for every 5,000 units in the batch, taken in approximately equal amounts from each container. The sample shall not be less than the minimum number of units specified in the appropriate monograph.

(iii) In the case of drugs packaged for repackaging or for use in the manufacture of another drug, the sample must be representative of the batch. Such samples may be taken from a composite composed of portions taken from a representative number of bulk containers, the composite consisting of

no more than 10 times the amount required for conducting the required tests and assays. Such samples are not required if they have been previously submitted.

(iv) In the case of a sterile drug packaged in combination with containers of a sterile diluent, the sample shall be collected by taking 20 immediate containers of the diluent collected at regular intervals throughout each filling operation, except that if the diluent is sterilized after filling into containers, the representative sample shall consist of 20 immediate containers collected from each sterilizer load and each container shall be taken from a different part of each such sterilizer load. In the case of sterile drugs packaged in combination with sterile droppers, the sample shall be collected by taking 20 droppers from each sterilizer load and each stopper shall be taken from a different part of such sterilizer load.

(9) In the case of an initial request for certification, each ingredient used in making the batch other than ingredients required by specific regulations: 1 package of each containing approximately 5 grams. Results and dates of the latest tests and assays made by or for him on such ingredients shall precede or accompany the submission.

(10) The results and dates of tests and assays made by or for him on the nonantibiotic active ingredients in the batch.

(11) If such batch or any part thereof is to be packaged with a sterile diluent or sterile dropper, such request shall also be accompanied by a statement that such diluent or dropper is sterile and conforms to the requirements prescribed therefor by specific regulations.

(d) Each sample submitted pursuant to the regulations in this chapter shall be addressed to the Commissioner. Its package shall be clearly identified as to its contents and shall bear the name and post-office address of the person submitting it.

(e) In addition to the information and samples specifically required to be submitted to the Commissioner by the regulations in this chapter, the person who requests certification of a batch shall submit such further information

and samples as the Commissioner may require for the purpose of investigations to determine whether or not such batch complies with the requirements of § 431.10 of this chapter for the issuance of a certificate.

(f) Upon the request of any person, stating reasonable grounds therefor, the Commissioner shall furnish such person with a portion of the working standards.

(Secs. 507, 512(n), 59 Stat. 463 as amended, 42 Stat. 350-351 (21 U.S.C. 357, 360b(n)))

(40 FR 13825, Mar. 27, 1975, as amended at 43 FR 41198, Sept. 15, 1978; 45 FR 40111, June 13, 1980)

§ 514.51 Certification of animal drugs subject to section 512(n) of the act.

(a) If it appears to the Commissioner, after such investigation as he considers necessary, that:

(1) The information (including results of tests and assays) and samples required by or pursuant to the regulations in this chapter have been submitted, and the request for certification contains no untrue statement of a material fact; and

(2) The batch complies with the regulations in this chapter and conforms to the applicable standards of identity, strength, quality, and purity prescribed by the regulations in this chapter;

the Commissioner shall certify that such batch is safe and efficacious for use, subject to such conditions on the effectiveness of certificates as are prescribed by § 431.11 of this chapter, and shall issue to the person who requested it a certificate to that effect.

(b) If the Commissioner determines, after such investigation as he considers to be necessary, that the information submitted pursuant to the regulations in this chapter, or the batch covered by such request, does not comply with the requirements set forth in paragraph (a) of this section for the issuance of a certificate, the Commissioner shall refuse to certify such batch and shall give notice thereof to the person who requested certification, stating his reasons for refusal.

(c) All statements, samples, and other information and materials submitted in connection with a request

for certification shall be considered to be part of such request.

(d) Compliance of a drug with the standards of identity, strength, quality, and purity prescribed by regulations in this chapter shall be determined by the tests and methods of assay prescribed for such drug by regulations issued under this chapter.

(e) The regulations in this chapter, prescribing tests and methods of assay for antibiotic and antibiotic-containing drugs, shall not be construed as preventing the Commissioner from using any other test or method of assay in his investigations to determine whether or not:

(1) A request for certification contains any untrue statement of a material fact; or

(2) A certification has been obtained through fraud, or through misrepresentation or concealment of a material fact.

(f) Except as specifically provided by the regulations in this chapter, no provision of any regulation shall be construed as exempting any certifiable antibiotic drug from any applicable provision of the act or any regulation thereunder.

(Sec. 507, 59 Stat. 463 as amended (21 U.S.C. 357))

§ 514.55 Forms for certification or exemption of antibiotic drugs for animal use subject to section 512(n) of the act.

The following forms which must be supplied in connection with certain certification or exemption procedures for antibiotic drugs for veterinary use may be obtained from the Certification Services Staff (HFD-145), Food and Drug Administration, Department of Health and Human Services, 5600 Fishers Lane, Rockville, MD 20857:

Form

- 1 Application for exemption for storage.
- 2 Application for exemption for processing.
- 3 Application for exemption for labeling.
- 4 Application for exemption for manufacturing use.
- 7 Request for check tests and assays or certification of a batch of _____ (the blank to be filled in with the name of the antibiotic drug).
- 8 Application for exemption for repackaging.
- 9 Request for supplemental certification of a batch of an antibiotic drug.

1900 Application for exemption for antibiotics mixed in animal feeds. Form FDA 1900 must be used when applications for medicated feeds rely for evidence of safety and effectiveness on a regulation published pursuant to section 512(i) of the act.

(Sec. 507, 59 Stat. 463 as amended (21 U.S.C. 357))

(40 FR 13825, Mar. 27, 1975, as amended at 51 FR 7391, Mar. 3, 1986)

§ 514.60 Fees for certification of animal drugs subject to section 512(n) of the act.

The fees for certification services for veterinary drugs are described in the applicable provisions of § 431.53 of this chapter.

(Secs. 507, 512(n), 59 Stat. 463 as amended, 62 Stat. 350-351 (21 U.S.C. 357-360b(n)))

(44 FR 67113, Nov. 23, 1979)

Subpart B—Administrative Actions on Applications

§ 514.100 Evaluation and comment on applications.

(a) After the filed application has been evaluated, the applicant will be furnished written comment on any apparent deficiencies in the application.

(b) When the description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such new animal drug appears adequate on its face, but it is not feasible to reach a conclusion as to the safety and effectiveness of the new animal drug solely from consideration of this description, the applicant may be notified that an establishment inspection is required to verify their adequacy.

(c) A request for samples of a new animal drug or any edible tissues and byproducts of animals treated with such a drug, shall specify the quantity deemed adequate to permit tests of analytical methods to determine their adequacy for regulatory purposes. The request should be made as early in the 180-day period as possible to assure timely completion. The date used for computing the 180-day limit for the purposes of section 512(c) of the act shall be moved forward 1 day for each day after the mailing date of the request until all of the requested sam-

ples are received. If the samples are not received within 90 days after the request, the application will be considered withdrawn without prejudice.

(d) The information contained in an application may be insufficient to determine whether a new animal drug is safe or effective in use if it fails to include (among other things) a statement showing whether such drug is to be limited to prescription sale and exempt under section 502(f) of the act from the requirement that its labeling bear adequate directions for lay use. If such drug is to be exempt, the information may also be insufficient if:

(1) The specimen labeling proposed fails to bear adequate information for professional use including indications, effects, dosages, routes, methods, and frequency and duration of administration and any relevant hazards, contraindications, side effects, and precautions under which practitioners licensed by law to administer such drug can use the drug for the purposes for which it is intended, including all purposes for which it is to be advertised, or represented, in accordance with § 201.105 of this chapter, and information concerning hazards, contraindications, side effects, and precautions relevant with respect to any uses for which such drug is to be prescribed.

(2) The application fails to show that the labeling and advertising of such drug will offer the drug for use only under those conditions for which it is offered in the labeling that is part of the application.

(3) The application fails to show that all labeling that furnishes or purports to furnish information for professional use of such drug will contain, in the same language and emphasis, the information for use including indications, effects, dosages, routes, methods, and frequency and duration of administration and any relevant warnings, hazards, contraindications, side effects, and precautions, which is contained in the labeling that is part of the application in accordance with § 201.105 of this chapter.

(e) The information contained in an application will be considered insufficient to determine whether a new animal drug is safe and effective for use when there is a refusal or failure

upon written notice to furnish inspectors authorized by the Food and Drug Administration an adequate opportunity to inspect the facilities, controls, and records pertinent to the application.

(f) On the basis of preliminary consideration of an application or supplemental application containing type-written or other draft labeling in lieu of final printed labeling, an applicant may be informed that such application is approvable when satisfactory final printed labeling identical in content to such draft copy is submitted.

(g) When an application has been found incomplete on the basis of a need for the kind of information described in § 514.6, such application shall be considered withdrawn without prejudice to future filing on the date of issuance of the letter citing the inadequacies contained in the application, unless within 30 days the sponsor chooses to avail himself of the opportunity for hearing as prescribed by § 514.111.

§ 514.105 Approval of applications.

(a) Within 180 days after an application has been filed pursuant to § 514.1, if the Commissioner determines that none of the grounds for denying approval specified in section 512(d) of the act applies:

(1) He shall forward for publication in the *FEDERAL REGISTER* a regulation prescribing the conditions under which the new animal drug may be used, including the name and address of the applicant; the conditions and indications for use covered by the application; any tolerance, withdrawal period, or other use restrictions; any tolerance required for the new animal drug substance or its metabolites in edible products of food-producing animals; and, if such new animal drug is intended for use in animal feed, appropriate purposes and conditions of use (including special labeling requirements) applicable to any animal feed; and such other information the Commissioner deems necessary to assure safe and effective use.

(2) He shall notify the applicant by sending him a copy of the proposed publication as described in paragraph (a)(1) of this section.

(b) Within 90 days after an application filed pursuant to § 514.2 if the Commissioner determines that none of the grounds for denying approval specified in section 512(m)(3) of the act applies, he shall notify the applicant that it is approvable by signing and mailing to the sponsor the original copy of the Form FDA 1900.

[40 FR 13825, Mar. 27, 1975, as amended at 51 FR 7392, Mar. 3, 1986]

§ 514.110 Reasons for refusing to file applications.

(a) The date of receipt of an application for a new animal drug shall be the date on which the application shall be deemed to be filed.

(b) An application for a new animal drug shall not be considered acceptable for filing for any of the following reasons:

(1) It does not contain complete and accurate English translations of any pertinent part in a foreign language.

(2) Fewer than three copies are submitted.

(3) It is incomplete on its face in that it is not properly organized and indexed.

(4) On its face the information concerning required matter is so inadequate that the application is clearly not approvable.

(5) The new animal drug is to be manufactured, prepared, propagated, compounded, or processed in whole or in part in any State in an establishment that has not been registered or exempted from registration under the provisions of section 510 of the act.

(6) The sponsor does not reside or maintain a place of business within the United States and the application has not been countersigned by an attorney, agent, or other representative of the applicant, which representative resides in the United States and has been duly authorized to act on behalf of the applicant and to receive communications on all matters pertaining to the application.

(7) The new animal drug is a drug subject to licensing under the animal virus, serum, and toxin law of March 4, 1913 (37 Stat. 832; 21 U.S.C. 151 et seq.). Such applications will be re-

ferred to the U.S. Department of Agriculture for action.

(8) It fails to include, with respect to each nonclinical laboratory study contained in the application, either a statement that the study was conducted in compliance with the good laboratory practice regulations set forth in Part 58 of this chapter, or, if the study was not conducted in compliance with such regulations, a brief statement of the reasons for the noncompliance.

(9) [Reserved]

(10) The applicant fails to submit a complete environmental assessment which addresses each of the items specified in the applicable format under § 25.31 of this chapter or fails to provide sufficient information to establish that the requested action is subject to categorical exclusion under § 25.24 of this chapter

(c) If an application is determined not to be acceptable for filing, the applicant shall be notified within 30 days of receipt of the application and shall be given the reasons therefore.

(d) If the applicant disputes the findings that his application is not acceptable for filing, he may make written request that the application be filed over protest, in which case it will be filed as of the day originally received.

(Secs. 406, 408, 409, 501, 502, 503, 505, 506, 507, 510, 512-516, 518-520, 601, 701, 706, and 801, 52 Stat. 1049-1053 as amended, 1055, 1056 as amended, 1058 as amended, 55 Stat. 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511-517 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 399-407 as amended, 76 Stat. 794 as amended, 82 Stat. 343-351, 90 Stat. 539-574 (21 U.S.C. 346, 346a, 348, 351, 352, 353, 355, 356, 357, 360, 360b-360f, 360h-360i, 371, 376); secs. 215, 301, 351, 354-360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 241, 262, 263b-263n))

[40 FR 13825, Mar. 27, 1975, as amended at 50 FR 7517, Feb. 22, 1985; 50 FR 16668, Apr. 26, 1985]

§ 514.111 Refusal to approve an application.

(a) The Commissioner shall, within 180 days after the filing of the application, inform the applicant in writing of his intention to issue a notice of opportunity for a hearing on a proposal to refuse to approve the application, if

the Commissioner determines upon the basis of the application, or upon the basis of other information before him with respect to a new animal drug, that:

(1) The reports of investigations required to be submitted pursuant to section 512(b) of the act do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; or

(2) The results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions; or

(3) The methods used in and the facilities and controls used for the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity; or

(4) Upon the basis of the information submitted to the Food and Drug Administration as part of the application, or upon the basis of any other information before it with respect to such drug, it has insufficient information to determine whether such drug is safe for use under such conditions. In making this determination the Commissioner shall consider, among other relevant factors:

(i) The probable consumption of such drug and of any substance formed in or on food because of the use of such drug;

(ii) The cumulative effect on man or animal of such drug, taking into account any chemically or pharmacologically related substances;

(iii) Safety factors which, in the opinion of experts qualified by scientific training and experience to evaluate the safety of such drugs, are appropriate for the use of animal experimentation data; and

(iv) Whether the conditions of use prescribed, recommended, or suggested in the proposed labeling are reasonably certain to be followed in practice; or

(5)(i) Evaluated on the basis of information submitted as part of the application and any other information before the Food and Drug Administra-

tion with respect to such drug, there is lack of substantial evidence consisting of adequate and well-controlled investigations, including clinical (field) investigation, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and reasonably be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling.

(ii) The following principles have been developed over a period of years and are recognized by the scientific community as the essentials of adequate and well-controlled clinical (field) investigations. They provide the basis for the determination whether there is "substantial evidence" to support the claims of effectiveness for "new animal drugs."

(a) The plan or protocol for the study and the report of the results of the effectiveness study must include the following:

(1) A clear statement of the objectives of the study.

(2) A method of selection of the subjects that—

(i) Provides adequate assurance that they are suitable for the purposes of the study, diagnostic criteria of the condition to be treated or diagnosed, confirmatory laboratory tests where appropriate, and, in the case of prophylactic agents, evidence of susceptibility and exposure to the condition against which prophylaxis is desired;

(ii) Assigns the subjects to test groups in such a way as to minimize bias; and

(iii) Assures comparability in test and control groups of pertinent variables, such as species, age, sex, duration and severity of disease, management practices, and use of drugs other than those being studied. When the effect of such variables is accounted for by an appropriate design, and when, within the same animal, effects due to the test drug can be obtained free of the effects of such variables, the same animal may be used for both the test drug and the control using the controls set forth in paragraph

(a)(5)(ii)(a)(4)(i), (ii), or (iii) of this section.

(3) An explanation of the methods of observation and recording of the animal response variable studied and the means of excluding bias or minimizing bias in the observations.

(4) A comparison of the results of treatment or diagnosis with a control in such a fashion as to permit quantitative evaluation. The precise nature of the control must be stated and an explanation given of the methods used to minimize bias on the part of the observers and the analysts of the data. Level and methods of "blinding," if used, are to be documented. Generally, four types of comparisons are recognized:

(i) No treatment: Where objective measurements of effectiveness are available and placebo effect is negligible, comparison of the objective results in comparable groups of treated and untreated animals.

(ii) Placebo control: Comparison of the results of use of the new animal drug entity with an inactive preparation designed to resemble the test drug as far as possible.

(iii) Active treatment control: An effective regimen of therapy may be used for comparison, e.g., where the condition treated is such that no treatment or administration of a placebo would be contrary to the well-being of the animals.

(iv) Historical control: In some circumstances involving diseases with high and predictable mortality (leukemia or tetanus) or with signs and symptoms of predictable duration or severity (some forms of parasitism, bovine hypocalcemia, canine eclampsia) or in the case of prophylaxis where morbidity is predictable, the results of use of a new animal drug entity may be compared quantitatively with prior experience historically derived from the adequately documented natural history of the disease or condition in comparable animals with no treatments or with a regimen (therapeutic, diagnostic, prophylactic) whose effectiveness is established.

(5) A summary of the methods of analysis and an evaluation of data derived from the study, including any appropriate statistical methods.

(6) Any of the criteria in this paragraph (a)(5)(ii) may be waived in whole or in part, either before the investigation or in the evaluation of a completed study, by the Director of the Bureau of Veterinary Medicine with respect to a specific clinical (field) investigation. A petition for such a waiver may be filed by any person who would be adversely affected by application of the criteria to a particular clinical investigation. The petition should show that some or all of the criteria are not reasonably applicable to the investigation and that alternative procedures can be or have been followed, the results of which will yield or have yielded data that can and should be accepted as substantial evidence of the drug's effectiveness. A petition for a waiver shall set forth clearly and concisely the specific provision or provisions in the criteria from which waiver is sought, why the criteria are not reasonably applicable to the particular clinical (field) investigation, what alternative procedures, if any, are to be or have been employed, what results have been obtained, and the basis on which it can be or has been concluded that the clinical (field) investigation will yield or has yielded substantial evidence of effectiveness, notwithstanding nonconformance with the criteria for which waiver is requested.

(b) Standardized test drug: For such an investigation to be considered adequate for consideration for approval of a new animal drug, the test drug must be standardized as to identity, strength, quality, purity, and dosage form to give significance to the results of the investigation.

(c) Uncontrolled studies or partially controlled studies are not acceptable as the sole basis for the approval of claims of effectiveness. Such studies, carefully conducted and documented, may provide corroborative support of well-controlled studies regarding efficacy and may yield valuable data regarding safety of the test drug. Such studies will be considered on their merits in the light of the principles listed here, with the exception of the requirement for the comparison of the treated subjects with controls. Isolated case reports, random experience, and

reports lacking the details which permit scientific evaluation will not be considered.

(6) Failure to include an appropriate proposed tolerance for residues in edible products derived from animals or a withdrawal period or other restrictions for use of such drug if any tolerance or withdrawal period or other restrictions for use are required in order to assure that the edible products derived from animals treated with such drug will be safe.

(7) Based on a fair evaluation of all material facts, the labeling is false or misleading in any particular; or

(8) Such drug induces cancer when ingested by man or animal or, after appropriate tests for evaluation of the safety of such drug, induces cancer in man or animal, except that this subparagraph shall not apply with respect to such drug if the Commissioner finds that, under the conditions of use specified in proposed labeling and reasonably certain to be followed in practice:

(i) Such drug will not adversely affect the animal for which it is intended; and

(ii) No residue of such drug will be found (by methods of examination prescribed or approved by the Commissioner by regulations) in any edible portion of such animal after slaughter or in any food yielded by, or derived from the living animals.

(9) The applicant fails to submit an adequate environmental assessment under § 25.31 of this chapter or fails to provide sufficient information to establish that the requested action is subject to categorical exclusion under § 25.24 of this chapter.

(10) The drug fails to satisfy the requirements of Subpart E of Part 500 of this chapter.

(11) Any nonclinical laboratory study that is described in the application and that is essential to show that the drug is safe for use under the conditions prescribed, recommended, or suggested in its proposed labeling, was not conducted in compliance with the good laboratory practice regulations as set forth in Part 58 of this chapter and no reason for the noncompliance is provided or, if it is, the differences between the practices used in conducting the study and the good laboratory

practice regulations do not support the validity of the study.

(b) The Commissioner shall within 90 days after the filing of the application inform the applicant in writing of his intention to issue a notice of opportunity for a hearing on a proposal to refuse to approve the application, if the Commissioner determines upon the basis of the application, or upon the basis of other information before him with respect to an animal feed bearing or containing a new animal drug that:

(1) There is not in effect a regulation established pursuant to section 512(i) of the act (identified in such application) on the basis of which such application may be approved; or

(2) Such animal feed (including the proposed use of any new animal drug therein or thereon) does not conform to an applicable regulation published pursuant to section 512(i) of the act (identified in such application), or that the purposes or conditions or indications of use prescribed, recommended, or suggested in the labeling of such feed do not conform to the applicable purposes and conditions or indications for use (including warnings) published pursuant to section 512(i) of the act or such labeling omits or fails to conform to other applicable information published pursuant to such section; or

(3) The methods used in and the facilities and controls used for the manufacturing, processing, and packaging of such animal feed are not adequate to preserve the identity, strength, quality, and purity of the new animal drug therein; or

(4) Based on a fair evaluation of all the material facts, such labeling is false or misleading in any particular.

(c) The Commissioner, as provided in § 514.200 of this chapter, shall expeditiously notify the applicant of an opportunity for a hearing on the question of whether such application is approvable, unless by the 30th day following the date of issuance of the letter informing the applicant of the intention to issue a notice of opportunity for a hearing the applicant:

(1) Withdraws the application; or

(2) Waives the opportunity for a hearing; or

(3) Agrees with the Commissioner on an additional period to precede issuance of such notice of hearing.

(Secs. 406, 408, 409, 501, 502, 503, 505, 506, 507, 510, 512-516, 518-520, 601, 701, 706, and 801, 52 Stat. 1049-1053 as amended, 1055, 1056 as amended, 1058 as amended, 55 Stat. 351 as amended, 59 Stat. 463 as amended, 68 Stat. 511-517 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 399-407 as amended, 76 Stat. 794 as amended, 82 Stat. 343-351, 90 Stat. 539-574 (21 U.S.C. 346, 346a, 348, 351, 352, 353, 355, 356, 357, 360, 360b-360f, 360h-360i, 371, 376); secs. 215, 351, 354-360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 241, 262, 263b-263n))

[40 FR 13825, Mar. 27, 1975, as amended at 43 FR 22675, May 26, 1978; 44 FR 16007, Mar. 16, 1979; 50 FR 7517, Feb. 22, 1985; 50 FR 16668, Apr. 26, 1985; 52 FR 49588, Dec. 31, 1987]

§ 514.112 Return of applications for animal feeds bearing or containing new animal drugs.

Applications submitted pursuant to § 514.2 will be returned to the applicant if such applications are incomplete or inaccurate or do not contain an identification of the applicable regulation(s). These regulations include those published pursuant to section 512(i) of the act, and are found in Part 558 of this chapter. In addition, § 510.515 of this chapter may also provide a basis on which approval of the application relies, as required by § 514.2(b)(10). All reasons for the return of the application will be made known to the applicant.

[51 FR 7392, Mar. 3, 1986]

§ 514.115 Withdrawal of approval of applications.

(a) The Secretary may suspend approval of an application approved pursuant to section 512(c) or (m)(2) of the act and give the applicant prompt notice of his action and afford the applicant the opportunity for an expedited hearing on a finding that there is an imminent hazard to the health of man or of the animals for which such new animal drug or animal feed is intended.

(b) The Commissioner shall notify in writing the person holding an application approved pursuant to section

512(c) or (m)(2) of the act and afford an opportunity for a hearing on a proposal to withdraw approval of such application if he finds:

(1) That the application contains any untrue statement of a material fact; or

(2) That the applicant has made any changes from the standpoint of safety or effectiveness beyond the variations provided for in the application unless he has supplemented the application by filing with the Secretary adequate information respecting all such changes and unless there is in effect an approval of the supplemental application, or such changes are those for which written authorization or approval is not required as provided for in § 514.8. The supplemental application shall be treated in the same manner as the original application.

(3) That in the case of an application for use of a new animal drug approved or deemed approved pursuant to section 512(c) of the act:

(i) Experience or scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved; or

(ii) New evidence not contained in such application or not available to the Secretary until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the Secretary when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved or that section 512 (d)(1)(H) of the act applies to such drug; or

(iii) On the basis of new information before him with respect to such drug, evaluated together with the evidence available to him when the application was approved, there is a lack of substantial evidence that such drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof.

(4) That any nonclinical laboratory study that is described in the application and that is essential to show that

the drug is safe for use under the conditions prescribed, recommended, or suggested in its proposed labeling, was not conducted in compliance with the good laboratory practice regulations as set forth in Part 58 of this chapter and no reason for the noncompliance is provided or, if it is, the differences between the practices used in conducting the study and the good laboratory practice regulations do not support the validity of the study.

(c) The Commissioner may notify in writing the person holding an application approved pursuant to section 512(c) or (m)(2) of the act and afford an opportunity for a hearing on a proposal to withdraw approval of such application if he finds:

(1) That the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports in accordance with a regulation or order under section 512(l)(1) or (m)(5)(A) of the act, or the applicant has refused to permit access to, or copying, or verification of, such records as required by section 512(l)(2) or (m)(5)(B) of the act; or

(2) That on the basis of new information before him evaluated together with the evidence before him when the application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of such drug or animal feed are inadequate to assure and preserve its identity, strength, quality, and purity and were not made adequate within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of; or

(3) That on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the labeling of such drug or animal feed, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of.

(d) Approval of an application pursuant to section 512(c) or (m)(2) of the act will be withdrawn on the basis of a

request for its withdrawal submitted in writing by a person holding an approved new animal drug application on the grounds that the drug subject to such application is no longer being marketed and information is included in support of this finding, provided none of the conditions cited in paragraphs (a), (b), and (c) of this section pertain to the subject drug. A written request for such withdrawal shall be construed as a waiver of the opportunity for a hearing as otherwise provided for in this section. Withdrawal of approval of an application under the provisions of this paragraph shall be without prejudice.

(e) On the basis of the withdrawal of approval of an application for a new animal drug approved pursuant to section 512(c) of the act, the regulation published pursuant to section 512(l) of the act covering the conditions of use of such drug as provided for in the application shall be revoked. An application providing for the manufacture of animal feeds bearing or containing such drug and approved pursuant to section 512(m)(2) of the act shall be deemed as withdrawn upon publication in the FEDERAL REGISTER of the order revoking the corresponding regulation.

(Secs. 406, 408, 409, 501, 502, 503, 505, 506, 507, 510, 512-516, 518-520, 601, 701, 706, and 801, 52 Stat. 1049-1053 as amended, 1055, 1056 as amended, 1058 as amended, 55 Stat. 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511-517 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 399-407 as amended, 76 Stat. 794 as amended, 82 Stat. 343-351, 90 Stat. 539-574 (21 U.S.C. 346, 346a, 348, 351, 352, 353, 355, 356, 357, 360, 360b-360f, 360h-360l, 371, 376); secs. 215, 301, 351, 354-360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 241, 262, 263b-263n))

[40 FR 13825, Mar. 27, 1975, as amended at 50 FR 7517, Feb. 22, 1985]

§ 514.116 Notice of withdrawal of approval of application.

When an approval of an application submitted pursuant to section 512 of the act is withdrawn by the Commissioner, he will give appropriate public notice of such action by publication in the FEDERAL REGISTER.

§ 514.120 Revocation of order refusing to approve an application or suspending or withdrawing approval of an application.

The Commissioner, upon his own initiative or upon request of an applicant stating reasonable grounds therefor and if he finds that the facts so require, may issue an order approving an application that previously has had its approval refused, suspended, or withdrawn.

§ 514.121 Service of notices and orders.

All notices and orders under this Subchapter E and section 512 of the act pertaining to new animal drug applications shall be served:

(a) In person by any officer or employee of the Department designated by the Commissioner; or

(b) By mailing the order by certified mail addressed to the applicant or respondent at his last known address in the records of the Food and Drug Administration.

§ 514.150 Conditions on the effectiveness of certificates for animal drugs subject to section 512(n) of the act.

(a) A certificate shall not become effective:

(1) If it is obtained through fraud or through misrepresentation or concealment of a material fact;

(2) With respect to any package unless it complies with the packaging requirements, if any, prescribed by the regulations in this chapter which were in effect on the date of the certificate;

(3) With respect to any package unless its label and labeling bear all words, statements, and other information required by the regulations in this chapter; or

(4) With respect to any package of a certifiable antibiotic drug subject to the regulations in this chapter, when it is included in a packaged combination with another drug, unless such other drug complies with the requirements of the regulations in this chapter.

(b) A certificate shall cease to be effective:

(1) With respect to any immediate container after the expiration date, if

any, prescribed by the regulations in this chapter;

(2) With respect to any immediate container when it or its seal (if the regulations in this chapter require it to be sealed) is broken, or when its label or labeling is altered, mutilated, destroyed, obliterated, or removed in whole or in part, or ceases to conform to any labeling requirement prescribed by the regulations in this chapter, except that:

(i) If the drug in such container is repacked or used as an ingredient in the manufacture of another drug, and certification of the batch thus made is requested, such certificate shall continue to be effective for a reasonable time to permit certification or destruction of such batch;

(ii) If the drug is in a container packaged for dispensing and is used in compounding a prescription issued by a practitioner licensed by law to administer such drug, such certificate shall continue to be effective for a reasonable time to permit the delivery of the drug compounded on such prescription; or

(iii) If its label or labeling is removed in whole or in part for the purpose of relabeling and supplemental certification of the relabeled drug is requested, as provided by § 433.12 of this chapter.

(3) With respect to any immediate container of penicillin when it is included in the packaged combination penicillin with aluminum hydroxide gel or penicillin with a vasoconstrictor, or to any immediate container of bacitracin when it is included in the packaged combination bacitracin with a vasoconstrictor, except that when certification of the batch so included is requested, such certificate shall continue to be effective for a reasonable time to permit certification of such batch which is part of such combination;

(4) With respect to any package when the drug therein fails to meet the standards of identity, strength, quality, and purity which were in effect on the date of the certificate; except that those minor changes which occur before the expiration date and which are normal and unavoidable in good storage and distribution practice shall be disregarded;

(5) With respect to any package of a certifiable antibiotic drug subject to the regulations in this chapter, included in a packaged combination with another drug, when such other drug fails to meet the requirements of the regulations in this chapter; or

(6) With respect to any immediate container, if such regulations require its labeling to bear a caution against dispensing otherwise than on prescription, at the beginning of the act of dispensing or offering to dispense it otherwise than:

(i) By a practitioner licensed by law to administer such drug; or

(ii) On his prescription issued in his professional practice.

(Sec. 507, 59 Stat. 463 as amended (21 U.S.C. 357))

§ 514.155 Suspension of certification service for sponsors of animal drugs.

When the Commissioner finds that a person has:

(a) Obtained or attempted to obtain a certificate through fraud or through misrepresentation or concealment of a material fact; or

(b) Falsified the records required to be kept by § 510.350 of this chapter; or

(c) Failed to keep such records or to make them available, or to accord full opportunity to take an inventory of stocks on hand, or otherwise to check the correctness of such records as required by § 510.350 of this chapter; or

(d) Failed to establish a system for maintaining the records required by § 510.300 of this chapter or has repeatedly or deliberately failed to maintain such records or to make required reports in accordance with the provisions of that section, or has refused to permit access to, or copying, or verification of such records or reports; or

(e) Failed to conform to the requirements of good manufacturing practice prescribed by Subchapter C of this chapter; the Commissioner will immediately suspend service to such person under the regulations in this chapter. Upon request a hearing will be granted to such person to show cause why such service should be resumed.

(Sec. 507, 59 Stat. 463 as amended (21 U.S.C. 357))

§ 514.160 Disposition of outdated animal drugs subject to section 512(n) of the act.

When certification becomes invalid because the expiration date is passed, such articles should not be disposed of for drug use either through commercial or charitable channels unless the articles have been assayed to establish potency and recertified.

(Sec. 507, 59 Stat. 463 as amended (21 U.S.C. 357))

Subpart C—Hearing Procedures

§ 514.200 Contents of notice of opportunity for a hearing.

(a) The notice to the applicant of opportunity for a hearing on a proposal by the Commissioner to refuse to approve an application or to withdraw the approval of an application will specify the grounds upon which he proposes to issue his order. On request of the applicant, the Commissioner will explain the reasons for his action. The notice of opportunity for a hearing will be published in the **FEDERAL REGISTER** and will specify that the applicant has 30 days after issuance of the notice within which he is required to file a written appearance electing whether:

- (1) To avail himself of the opportunity for a hearing; or
- (2) Not to avail himself of the opportunity for a hearing.

(b) If the applicant fails to file a written appearance in answer to the notice of opportunity for hearing, his failure will be construed as an election not to avail himself of the opportunity for the hearing, and the Commissioner without further notice may enter a final order.

(c) If the applicant elects to avail himself of the opportunity for a hearing, he is required to file a written appearance requesting the hearing within 30 days after the publication of the notice, giving the reason why the application should not be refused or should not be withdrawn, together with a well-organized and full-factual analysis of the clinical and other investigational data he is prepared to prove in support of his opposition to the Commissioner's proposal. A re-

quest for a hearing may not rest upon mere allegations or denials, but must set forth specific facts showing there is a genuine and substantial issue of fact that requires a hearing. When it clearly appears from the data in the application and from the reasons and a factual analysis in the request for the hearing that no genuine and substantial issue of fact precludes the refusal to approve the application or the withdrawal of approval of the application (for example, no adequate and well-controlled clinical investigations to support the claims of effectiveness have been identified), the Commissioner will enter an order on this data, stating his findings and conclusions. If a hearing is requested and is justified by the applicant's response to the notice of opportunity for a hearing, the issues will be defined, an Administrative Law Judge will be named, and he shall issue a written notice of the time and place at which the hearing will commence. In the case of denial of approval, such time shall be not more than 90 days after the expiration of such 30 days unless the Administrative Law Judge and the applicant otherwise agree; and, in the case of withdrawal of approval, such time shall be as soon as practicable.

(d) The hearing will be open to the public; however, if the Commissioner finds that portions of the application which serve as a basis for the hearing contain information concerning a method or process entitled to protection as a trade secret, the part of the hearing involving such portions will not be public, unless the respondent so specifies in his appearance.

(Sec. 701(a), 52 Stat. 1056 (21 U.S.C. 371(a))
[40 FR 13825, Mar. 27, 1975, as amended at 43 FR 1941, Jan. 13, 1978]

§ 514.201 Procedure for hearings.

Hearings relating to new animal drugs under section 512 (d), (e), (m)(3), and (m)(4) of the act shall be governed by Part 12 of this chapter.

[42 FR 4717, Jan. 25, 1977, as amended at 42 FR 10980, Feb. 25, 1977; 42 FR 15675, Mar. 22, 1977]

§ 514.210

§ 514.210 Hearing procedure.

Hearings pursuant to § 514.155 shall be governed by Part 16 of this chapter.

[41 FR 48268, Nov. 2, 1976, as amended at 42 FR 15875, Mar. 22, 1977]

Subparts D—E [Reserved]

Subpart F—Judicial Review

§ 514.235 Judicial review.

(a) The transcript and record shall be certified by the Commissioner. In any case in which the Commissioner enters an order without a hearing pursuant to § 314.200(g) of this chapter, the request(s) for hearing together with the data and information submitted and the Commissioner's findings and conclusions shall be included in the record certified by the Commissioner.

(b) Judicial review of an order withdrawing approval of a new drug application, whether or not a hearing has been held, may be sought by a manufacturer or distributor of an identical, related, or similar drug product, as defined in § 310.6 of this chapter, in a United States court of appeals pursuant to section 505(h) of the act.

[42 FR 4717, Jan. 25, 1977]

PART 520—ORAL DOSAGE FORM NEW ANIMAL DRUGS NOT SUBJECT TO CERTIFICATION

Sec.

- 520.23 Acepromazine maleate tablets.
- 520.44 Acetazolamide sodium soluble powder.
- 520.48 Altrenogest solution.
- 520.62 Aminopentamide hydrogen sulphate tablets.
- 520.82 Aminopropazine fumarate oral dosage forms.
- 520.82a Aminopropazine fumarate tablets.
- 520.82b Aminopropazine fumarate, neomycin sulfate tablets.
- 520.100 Amprolium oral dosage forms.
- 520.100a Amprolium drinking water.
- 520.100b Amprolium drench.
- 520.100c Amprolium crumbles.
- 520.110 Apramycin sulfate soluble powder.
- 520.182 Bicyclohexylammonium fumagillin.
- 520.222 Bunamidine hydrochloride.
- 520.240 Butonate liquid.

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- 520.246 Butorphanol tartrate tablets.
- 520.280 n-Butyl chloride capsules.
- 520.300 Cambendazole oral dosage forms.
- 520.300a Cambendazole suspension.
- 520.300b Cambendazole pellets.
- 520.300c Cambendazole paste.
- 520.310 Caramiphen ethanedisulfonate and ammonium chloride tablets.
- 520.314 Cefadroxil tablets.
- 520.315 Cefadroxil powder for oral suspension.
- 520.420 Chlorothiazide tablets and boluses.
- 520.434 Chlorphenesin carbamate tablets.
- 520.443 Chlorpromazine hydrochloride.
- 520.446 Clindamycin hydrochloride capsules.
- 520.447 Clindamycin hydrochloride liquid.
- 520.462 Clorsulon drench.
- 520.500 Coumaphos crumbles.
- 520.530 Cythioate oral liquid.
- 520.531 Cythioate tablets.
- 520.540 Dexamethasone oral dosage forms.
- 520.540a Dexamethasone powder.
- 520.540b Dexamethasone tablets and boluses.
- 520.540c Dexamethasone chewable tablets.
- 520.550 Dextrose/glycine/electrolyte.
- 520.563 Diatrizoate meglumine and diatrizoate sodium oral solution.
- 520.580 Dichlorophene and toluene capsules.
- 520.600 Dichlorvos.
- 520.620 Diethylcarbamazepine oral dosage forms.
- 520.620a Diethylcarbamazepine.
- 520.620b Diethylcarbamazepine chewable tablets.
- 520.622 Diethylcarbamazepine citrate oral dosage forms.
- 520.622a Diethylcarbamazepine citrate tablets.
- 520.622b Diethylcarbamazepine citrate syrup.
- 520.622c Diethylcarbamazepine citrate chewable tablets.
- 520.622d Diethylcarbamazepine citrate capsules.
- 520.623 Diethylcarbamazepine citrate, oxibendazole chewable tablets.
- 520.704 Diphenylhydantoin sodium capsules.
- 520.763 Dithiazanine iodide oral dosage forms.
- 520.763a Dithiazanine iodide tablets.
- 520.763b Dithiazanine iodide powder.
- 520.763c Dithiazanine iodide and piperazine citrate suspension.
- 520.784 Doxylamine succinate tablets.
- 520.812 Enrofloxacin tablets.
- 520.823 Erythromycin phosphate.
- 520.863 Ethylisobutrazine hydrochloride tablets.
- 520.903 Febantel oral dosage forms.
- 520.903a Febantel paste.
- 520.903b Febantel suspension.
- 520.903c Febantel-trichlorfon paste.

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- 520.903d Febantel-praziquantel paste.
- 520.905 Fenbendazole oral dosage forms.
- 520.905a Fenbendazole suspension.
- 520.905b Fenbendazole granules.
- 520.905c Fenbendazole paste.
- 520.905d Fenbendazole powder.
- 520.905e Fenbendazole blocks.
- 520.960 Flumethasone tablets.
- 520.970 Flunixin oral dosage forms.
- 520.970a Flunixin meglumine granules.
- 520.970b Flunixin meglumine paste.
- 520.1010 Furosemide oral dosage forms.
- 520.1010a Furosemide tablets or boluses.
- 520.1010b Furosemide powder.
- 520.1010c Furosemide syrup.
- 520.1044 Gentamicin sulfate oral dosage forms.
- 520.1044a Gentamicin sulfate oral solution.
- 520.1044b Gentamicin sulfate pig pump oral solution.
- 520.1044c Gentamicin sulfate soluble powder.
- 520.1065 Glycobiol tablets.
- 520.1100 Griseofulvin.
- 520.1120 Haloxon oral dosage forms.
- 520.1120a Haloxon drench.
- 520.1120b Haloxon boluses.
- 520.1157 Iodinated casein tablets.
- 520.1158 Iodochlorhydroxyquin boluses.
- 520.1182 Iron dextran oral suspension.
- 520.1192 Ivermectin paste.
- 520.1193 Ivermectin tablets.
- 520.1194 Ivermectin drench.
- 520.1195 Ivermectin liquid.
- 520.1204 Kanamycin sulfate, aminopentamide hydrogen sulfate, pectin, bismuth subcarbonate, activated attapulgit oral.
- 520.1236 Lenperone tablets.
- 520.1242 Levamisole hydrochloride oral dosage forms.
- 520.1242a Levamisole hydrochloride drench and drinking water.
- 520.1242b Levamisole hydrochloride tablet or oblet (bolus).
- 520.1242c Levamisole hydrochloride—piperazine dihydrochloride.
- 520.1242d Levamisole resinate.
- 520.1242e Levamisole hydrochloride effervescent tablets.
- 520.1242f Levamisole hydrochloride gel.
- 520.1242g Levamisole resinate and famphur paste.
- 520.1263 Lincomycin hydrochloride monohydrate oral dosage forms.
- 520.1263a Lincomycin hydrochloride monohydrate tablets and sirup.
- 520.1263b Lincomycin hydrochloride monohydrate and spectinomycin sulfate tetrahydrate soluble powder.
- 520.1263c Lincomycin hydrochloride soluble powder.
- 520.1284 Sodium liothyronine tablets.
- 520.1320 Mebendazole oral.
- 520.1326 Mebendazole and trichlorfon oral dosage forms.
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- 520.1326a Mebendazole and trichlorfon powder.
- 520.1326b Mebendazole and trichlorfon paste.
- 520.1330 Meclofenamic acid granules.
- 520.1331 Meclofenamic acid tablets.
- 520.1341 Megestrol acetate tablets.
- 520.1380 Methocarbamol tablets.
- 520.1409 Methylprednisolone, aspirin tablets.
- 520.1408 Methylprednisolone tablets.
- 520.1422 Metoserpate hydrochloride.
- 520.1430 Mibolerone.
- 520.1448 Monensin oral dosage forms.
- 520.1448a Monensin blocks.
- 520.1448b Monensin-mineral granules.
- 520.1450 Morantel tartrate oral dosage forms.
- 520.1450a Morantel tartrate bolus.
- 520.1450b Morantel tartrate cartridge.
- 520.1468 Naproxen granules.
- 520.1520 Niclosamide tablets.
- 520.1560 Nitrofurantoin oral dosage forms.
- 520.1560a Nitrofurantoin oral suspension.
- 520.1560b Nitrofurantoin tablets and boluses.
- 520.1628 Oxfendazole powder and pellets.
- 520.1629 Oxfendazole paste.
- 520.1630 Oxfendazole suspension.
- 520.1631 Oxfendazole and trichlorfon paste.
- 520.1638 Oxibendazole paste.
- 520.1640 Oxibendazole suspension.
- 520.1660 Oxytetracycline.
- 520.1660a Oxytetracycline and carbomycin in combination.
- 520.1660b Oxytetracycline hydrochloride capsules.
- 520.1660c Oxytetracycline hydrochloride tablets.
- 520.1660d Oxytetracycline hydrochloride soluble powder.
- 520.1720 Phenylbutazone oral dosage forms.
- 520.1720a Phenylbutazone tablets and boluses.
- 520.1720b Phenylbutazone granules.
- 520.1720c Phenylbutazone paste.
- 520.1720d Phenylbutazone gel.
- 520.1760 Phthalofyne tablets.
- 520.1780 Piperacetazine tablets.
- 520.1801 Piperazine adipate oral dosage forms.
- 520.1801a Piperazine adipate powder.
- 520.1802 Piperazine-carbon disulfide complex oral dosage forms.
- 520.1802a Piperazine-carbon disulfide complex suspension.
- 520.1802b Piperazine-carbon disulfide complex boluses.
- 520.1803 Piperazine citrate capsules.
- 520.1804 Piperazine phosphate capsules.
- 520.1805 Piperazine phosphate with thium cloylate tablets.

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 520.1806 Piperazine monohydrochloride liquid.
 520.1840 Poloxalene.
 520.1846 Polyoxyethylene (23) lauryl ether blocks.
 520.1870 Praziquantel tablets.
 520.1900 Primidone tablets.
 520.1920 Prochlorperazine, isopropamide sustained release capsules.
 520.1921 Prochlorperazine, isopropamide, with neomycin sustained-release capsules.
 520.1962 Promazine hydrochloride.
 520.2002 Propiopromazine hydrochloride.
 520.2022 Protokylol hydrochloride tablets.
 520.2041 Pyrantel pamoate chewable tablets.
 520.2042 Pyrantel pamoate tablets.
 520.2043 Pyrantel pamoate suspension.
 520.2044 Pyrantel pamoate paste.
 520.2045 Pyrantel tartrate powder; pyrantel tartrate pellets.
 520.2080 Ronnel oral dosage forms.
 520.2080a Ronnel blocks.
 520.2080b Ronnel tablets.
 520.2087 Roxarsone soluble powder.
 520.2088 Roxarsone tablets.
 520.2100 Selenium, vitamin E capsules.
 520.2122 Spectinomycin dihydrochloride oral solution.
 520.2123 Spectinomycin dihydrochloride pentahydrate oral dosage forms.
 520.2123a Spectinomycin dihydrochloride pentahydrate tablets.
 520.2123b Spectinomycin dihydrochloride pentahydrate soluble powder.
 520.2150 Stanozolol oral dosage forms.
 520.2150a Stanozolol tablets.
 520.2150b Stanozolol chewable tablets.
 520.2155 Starch, pregelatinized.
 520.2160 Styrylpyridinium, diethylcarbamazine oral dosage forms.
 520.2160a Styrylpyridinium, diethylcarbamazine tablets.
 520.2160b Styrylpyridinium chloride, diethylcarbamazine (as base).
 520.2160c Styrylpyridinium, diethylcarbamazine edible tablets.
 520.2160d Styrylpyridinium, diethylcarbamazine film-coated tablets.
 520.2170 Sulfabromomethazine sodium boluses.
 520.2184 Sodium sulfachloropyrazine monohydrate.
 520.2200 Sulfachlorpyridazine oral dosage forms.
 520.2200a Sulfachlorpyridazine bolus.
 520.2200b Sulfachlorpyridazine medicated milk and drinking water.
 520.2200c Sulfachlorpyridazine tablets.
 520.2220 Sulfadimethoxine oral dosage forms.
 520.2220a Sulfadimethoxine drinking water and drench.

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 520.2220b Sulfadimethoxine tablets and boluses.
 520.2220c Sulfadimethoxine oral suspension.
 520.2240 Sulfaethoxypyridazine.
 520.2240a Sulfaethoxypyridazine drinking water.
 520.2240b Sulfaethoxypyridazine tablets.
 520.2260 Sulfamethazine oral dosage forms.
 520.2260a Sulfamethazine tablets.
 520.2260b Sulfamethazine sustained-release boluses.
 520.2260c Sulfamethazine sustained-release tablets.
 520.2261 Sulfamethazine sodium oral dosage forms.
 520.2261a Sulfamethazine sodium drinking water solution.
 520.2261b Sulfamethazine sodium soluble powder.
 520.2280 Sulfamethizole and methenamine mandelate tablets.
 520.2320 Sulfanitran and aklomide in combination.
 520.2325 Sulfaquinoxaline oral dosage forms.
 520.2325a Sulfaquinoxaline drinking water.
 520.2325b Sulfaquinoxaline drench.
 520.2330 Sulfisoxazole tablets.
 520.2362 Thienium cloylate tablets.
 520.2380 Thiabendazole oral dosage forms.
 520.2380a Thiabendazole top dressing and mineral protein feed block.
 520.2380b Thiabendazole drench or oral paste.
 520.2380c Thiabendazole bolus.
 520.2380d Thiabendazole, piperazine citrate suspension.
 520.2380e Thiabendazole with trichlorfon.
 520.2380f Thiabendazole, piperazine phosphate powder.
 520.2455 Tiamulin.
 520.2460 Ticarbodine oral dosage forms.
 520.2460a Ticarbodine tablets.
 520.2460b Ticarbodine capsules.
 520.2473 Tioxidazole oral dosage forms.
 520.2473a Tioxidazole granules.
 520.2473b Tioxidazole paste.
 520.2480 Triamcinolone tablets.
 520.2481 Triamcinolone acetonide tablets.
 520.2482 Triamcinolone acetonide oral powder.
 520.2520 Trichlorfon oral dosage forms.
 520.2520a Trichlorfon oral.
 520.2520b Trichlorfon and atropine.
 520.2520c Trichlorfon oral liquid.
 520.2520d Trichlorfon paste.
 520.2520e Trichlorfon boluses.
 520.2520f Trichlorfon granules.
 520.2520g Trichlorfon, phenothiazine, and piperazine dihydrochloride powder.
 520.2520h Trichlorfon and phenothiazine powder.

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 520.2562 Trifluopromazine hydrochloride tablets.
 520.2604 Trimeprazine tartrate and prednisolone tablets.
 520.2605 Trimeprazine tartrate and prednisolone capsules.
 520.2610 Trimethoprim and sulfadiazine tablets.
 520.2611 Trimethoprim and sulfadiazine oral paste.
 520.2612 Trimethoprim and sulfadiazine oral suspension.
 520.2640 Tylosin.

AUTHORITY: Sec. 512(i), 82 Stat. 347 (21 U.S.C. 360b(i)); 21 CFR 5.10 and 5.83.

SOURCE: 40 FR 13838, Mar. 27, 1975, unless otherwise noted.

§ 520.23 Acepromazine maleate tablets.

(a) *Sponsors.* See drug labeler codes in § 510.600(c) of this chapter for identification of sponsors as follows:

(1) For No. 000856, use of 5-, 10-, or 25-milligram tablets as in paragraph (b) of this section.

(2) For Nos. 000725 and 054273, use of 10- or 25-milligram tablets as in paragraph (c) of this section.

(b) *Conditions of use.* It is used in dogs and cats as follows:

(1) *Indications for use.* It is used in dogs and cats as a tranquilizer.

(2) *Amount.* Dogs: 0.25 to 1.0 milligram per pound of body weight; Cats: 0.5 to 1.0 milligram per pound of body weight.

(3) *Limitations.* The drug is administered orally. Dosage may be repeated as required. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(c) *Conditions of use.* It is used in dogs as follows:

(1) *Indications for use.* It is used in dogs as an aid in tranquilization and as a preanesthetic agent.

(2) *Amount.* Dogs: 0.25 to 1.0 milligram per pound of body weight.

(3) *Limitations.* The drug is administered orally. Dosage may be repeated as required. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

46 FR 44443, Sept. 4, 1981, as amended at 50 FR 49091, Dec. 18, 1984; 52 FR 666, Jan. 1, 1987; 53 FR 40727, Oct. 18, 1988]

§ 520.44 Acetazolamide sodium soluble powder.

(a) *Specifications.* The drug is in a powder form containing acetazolamide sodium, USP equivalent to 25 percent acetazolamide activity.

(b) *Sponsor.* See No. 010042 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is used in dogs as an aid in the treatment of mild congestive heart failure and for rapid reduction of intraocular pressure.¹

(2) It is administered orally at a dosage level of 5 to 15 milligrams per pound of body weight daily.¹

(3) For use only by or on the order of a licensed veterinarian.¹

§ 520.48 Altrenogest solution.

(a) *Specifications.* Each milliliter of altrenogest solution contains 2.2 milligrams of altrenogest.

(b) *Sponsor.* See No. 012579 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* Administer orally at the rate of 1 milliliter per 100 pounds body weight (0.05 milligram per kilogram body weight). Give one dose daily for 15 consecutive days.

(2) *Indications for use.* For suppression of estrus in mares.

(3) *Limitations.* For oral use in horses only; avoid contact with the skin. Do not administer to horses intended for use as food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[48 FR 40887, Sept. 12, 1983]

§ 520.62 Aminopentamide hydrogen sulphate tablets.

(a) *Chemical name.* 4-(Dimethylamino)-2,2-diphenylvaleramide hydrogen sulfate.

(b) *Specifications.* Each tablet contains 0.2 milligram of the drug.

(c) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(d) *Conditions of use.* (1) It is intended for use in dogs and cats only

¹ These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

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for the treatment of vomiting and/or diarrhea, nausea, acute abdominal visceral spasm, pylorospasm, or hypertrophic gastritis.

NOTE: Not for use in animals with glaucoma because of the occurrence of mydriasis.

(2) Dosage is administered by oral tablet every 8 to 12 hours, as follows:

Weight of animal in pounds	Dosage in milligrams
Up to 10.....	0.1
11 to 20.....	0.2
21 to 50.....	0.3
51 to 100.....	0.4
Over 100.....	0.5

Dosage may be gradually increased up to a maximum of five times the suggested dosage. Oral administration of tablets may be preceded by subcutaneous or intramuscular use of the injectable form of the drug.

(3) For use only by or on the order of a licensed veterinarian.

[40 FR 13838, Mar. 27, 1975, as amended at 53 FR 27851, July 25, 1988]

§ 520.82 Aminopropazine fumarate oral dosage forms.

§ 520.82a Aminopropazine fumarate tablets.

(a) *Specifications.* The drug is in tablet form. Each tablet contains aminopropazine fumarate equivalent to 25 milligrams of aminopropazine base.

(b) *Sponsor.* See No. 017220 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used in dogs and cats for reducing excessive smooth muscle contractions, such as occur in urethral spasms associated with urolithiasis.¹

(2) It is administered at a dosage level of 1 to 2 milligrams per pound of body weight. The dosage can be repeated every 12 hours, as indicated.¹

(3) Not for use in animals intended for food purposes.

(4) For use only by or on the order of a licensed veterinarian.¹

[40 FR 13838, Mar. 27, 1975, as amended at 46 FR 48642, Oct. 2, 1981]

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§ 520.82b Aminopropazine fumarate, neomycin sulfate tablets.

(a) *Specifications.* The drug is in tablet form. Each tablet contains both aminopropazine fumarate equivalent to 25 milligrams of aminopropazine base and neomycin sulfate equivalent to 50 milligrams of neomycin base.

(b) *Sponsor.* See No. 017220 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used in dogs to control bacterial diarrhea caused by organisms susceptible to neomycin and to reduce smooth muscle contractions.¹

(2) It is administered at a dosage level of one to two tablets per 10 pounds of body weight twice daily for 3 days.¹

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

[40 FR 13838, Mar. 27, 1975, as amended at 46 FR 48642, Oct. 2, 1981]

§ 520.100 Amprolium oral dosage forms.

§ 520.100a Amprolium drinking water.

(a) *Chemical name.* 1-(4-Amino-2-n-propyl-5-pyrimidinylmethyl)-2-picolinium chloride hydrochloride.

(b) *Sponsor.* See No. 000006 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See § 556.50 of this chapter.

(d) *Conditions of use.* It is used in drinking water as follows:

(i) *Chickens and turkeys—(1) Amount.* 20 percent soluble powder.

(ii) *Indications for use.* Treatment of coccidiosis.

(iii) *Limitations.* Administer at the 0.012 percent level in drinking water as soon as coccidiosis is diagnosed and continue for from 3 to 5 days (in severe outbreaks, give amprolium at the 0.024 percent level); continue with 0.006 percent amprolium-medicated water for an additional 1 to 2 weeks; no other source of drinking water

¹These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

should be available to the birds during this time; as sole source of amprolium.

(2) *Calves*—(i) *Amount*. 9.6 percent solution or 20 percent soluble powder.

(a) *Indications for use*. As an aid in the treatment of coccidiosis caused by *Eimeria bovis* and *E. zurnii*.

(b) *Limitations*. Add 16 fluid ounces of the 9.6 percent solution to each 100 gallons of drinking water; or 4 ounces of the soluble powder to each 50 gallons of drinking water; at the usual rate of water consumption, this will provide an intake of approximately 10 milligrams per kilogram (2.2 pounds) of body weight; offer this solution as the only source of water for 5 days; for a satisfactory diagnosis, a microscopic examination of the feces should be done by a veterinarian or diagnostic laboratory before treatment; when treating outbreaks, the drug should be administered promptly after diagnosis is determined; withdraw 24 hours before slaughter.

(ii) *Amount*. 9.6 percent solution or 20 percent soluble powder.

(a) *Indications for use*. As an aid in the prevention of coccidiosis caused by *Eimeria bovis* and *E. zurnii*.

(b) *Limitations*. Add 8 fluid ounces of the 9.6 percent solution or 4 ounces of the 20 percent soluble powder to each 100 gallons of drinking water; at the usual rate of water consumption, this will provide an intake of approximately 5 milligrams per kilogram (2.2 pounds) of body weight; offer this solution as the only source of water for 21 days during periods of exposure or when experience indicates that coccidiosis is likely to be a hazard; withdraw 24 hours before slaughter.

§ 520.100b Amprolium drench.

(a) *Chemical name*. 1-(4-Amino-2-n-propyl-5-pyrimidinylmethyl)-2-picolinium chloride hydrochloride.

(b) *Sponsor*. See No. 000006 in § 510.600(c) of this chapter.

(c) *Related tolerances*. See § 556.50 of this chapter.

(d) *Conditions of use*. It is used for calves as follows:

(1) *Amount*. 9.6 percent solution or 20 percent soluble powder.

(i) *Indications for use*. As an aid in the treatment of coccidiosis caused by *Eimeria bovis* and *E. zurnii*.

(ii) *Limitations*. Add 3 fluid ounces of the 9.6 percent solution to 1 pint of water or 3 ounces of the 20 percent soluble powder to each quart of water and with a dose syringe administer 1 fluid ounce of this solution for each 100 pounds of body weight; this will provide a dose of approximately 10 milligrams per kilogram (2.2 pounds) of body weight; administer daily for 5 days; for a satisfactory diagnosis, a microscopic examination of the feces should be done by a veterinarian or diagnostic laboratory before treatment; when treating outbreaks, the drug should be administered promptly after diagnosis is determined; withdraw 24 hours before slaughter.

(2) *Amount*. 9.6 percent solution or 20 percent soluble powder.

(i) *Indications for use*. As an aid in the prevention of coccidiosis caused by *Eimeria bovis* and *E. zurnii*.

(ii) *Limitations*. Add 1½ fluid ounces of the 9.6 percent solution to 1 pint of water or 1½ ounces of the 20 percent soluble powder to each quart of water and with a dose syringe administer 1 fluid ounce of this solution for each 100 pounds of body weight; this will provide a dose of approximately 5 milligrams per kilogram (2.2 pounds) of body weight; administer daily for 21 days during periods of exposure or when experience indicates that coccidiosis is likely to be a hazard; withdraw 24 hours before slaughter.

§ 520.100c Amprolium crumbles.

(a) *Specifications*. Amprolium crumbles contain 1.25 percent amprolium.

(b) *Sponsor*. See No. 000006 in § 510.600(c) of this chapter.

(c) *Related tolerances*. See § 556.50 of this chapter.

(d) *Conditions of use*. It is top-dressed on or thoroughly mixed in the daily feed ration of calves as follows:

(1) *Amount*. 1.6 ounces of crumbles per 250 pounds of body weight per day (5 milligrams per kilogram of body weight).

(i) *Indications for use*. As an aid in the prevention of coccidiosis caused by *Eimeria bovis* and *E. zurnii*.

(ii) *Limitations*. Administer for 21 consecutive days during periods of exposure or when experience indicates

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that coccidiosis is likely to be a hazard. Withdraw 24 hours before slaughter. Use as sole source of amprolium.

(2) *Amount.* 3.2 ounces of crumbles per 250 pounds of body weight per day (10 milligrams per kilogram of body weight).

(i) *Indications for use.* As an aid in the treatment of coccidiosis caused by *Eimeria bovis* and *E. zurnii*.

(ii) *Limitations.* Administer for 5 consecutive days. For satisfactory diagnosis, a microscopic fecal examination should be done by a veterinarian or diagnostic laboratory before treatment. When treating outbreaks, the drug should be administered promptly after diagnosis is determined. Withdraw 24 hours before slaughter. Use as sole source of amprolium.

(Sec. 512(i), 82 Stat. 347 (21 U.S.C. 360b(i)) [42 FR 41855, Aug. 19, 1977]

§ 520.110 Apramycin sulfate soluble powder.

(a) *Specifications.* A water soluble powder used to make a medicated drinking water containing apramycin sulfate equivalent to 0.375 gram of apramycin activity per gallon of drinking water.

(b) *Sponsor.* See No. 000986 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See § 556.52 of this chapter.

(d) *Conditions of use.* (1) In swine for control of porcine colibacillosis (weanling pig scours) caused by strains of *E. coli* sensitive to apramycin.

(2) It is administered for 7 days in drinking water at the rate of 12.5 milligrams of apramycin per kilogram (5.7 milligrams per pound) of body weight per day. Swine will normally consume 1 gallon per day of medicated water containing 375 milligrams of apramycin for each 66 pounds of body weight. Water consumption should be monitored to determine that the required amount of apramycin is being consumed. The drug concentration should be adjusted according to water consumption which varies depending on ambient temperature, humidity, and other factors.

(3) Prepare fresh medicated water daily.

(4) Do not slaughter treated swine for 28 days following treatment

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[47 FR 15771, Apr. 13, 1982, as amended at 49 FR 19642, May 9, 1984; 53 FR 37753, Sept. 28, 1988]

§ 520.182 Bicyclohexylammonium fumagillin.

(a) *Specifications.* The drug is a soluble powder containing bicyclohexylammonium fumagillin and appropriate phosphate buffers.

(b) *Sponsor.* See No. 043731 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used for the prevention of nosema in honey bees.¹

(2) It is administered usually in a 2:1 sugar sirup containing a concentration of from 75 to 100 milligrams of fumagillin activity per gallon of sugar sirup.¹

(3) Colonies used for package production should be fed medicated sirup as a principal food supply for a month prior to stocking nuclei or shaking packages for market.¹

(4) The medicated sirup should not be fed immediately before or during the honey flow.

[40 FR 13838, Mar. 27, 1975, as amended at 42 FR 65151, Dec. 30, 1977]

§ 520.222 Bunamidine hydrochloride.

(a) *Chemical name.* *N,N*-Dibutyl-4-(hexyloxy)-1-naphthamidine hydrochloride.

(b) *Specifications.* The drug is an oral tablet containing 100, 200, or 400 milligrams of bunamidine hydrochloride.

(c) *Sponsor.* See No. 017220 in § 510.600(c) of this chapter.

(d) *Conditions of use.* (1) The drug is intended for oral administration to dogs for the treatment of the tapeworms *Dipylidium caninum*, *Taenia pisiformis*, and *Echinococcus granulosus*, and to cats for the treatment of the tapeworms *Dipylidium caninum* and *Taenia taeniaeformis*.

(2) It is administered to cats and dogs at the rate of 25 to 50 milligrams

¹ These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

per kilogram of body weight. The drug should be given on an empty stomach and food should not be given for 3 hours following treatment.

(3) Tablets should not be crushed, mixed with food, or dissolved in liquid. Repeat treatments should not be given within 14 days. The drug should not be given to male dogs within 28 days prior to their use for breeding. Do not administer to dogs or cats having known heart conditions.

(4) For use only by or on the order of a licensed veterinarian.

[40 FR 13838, Mar. 27, 1975, as amended at 42 FR 13018, Mar. 8, 1977; 46 FR 48642, Oct. 2, 1981]

§ 520.240 Butonate liquid.

(a) *Chemical name.* O,O-Dimethyl (2,2,2-trichloro-1-n-butyl oxyethyl) phosphonate.

(b) *Specifications.* Butonate liquid veterinary contains 13 percent butonate by weight in a suitable base.

(c) *Sponsor.* See No. 011536 in § 510.600(c) of this chapter.

(d) *Conditions of use.* (1) It is used in horses other than foals (sucklings and young weanlings) for the removal and control of bots (*Gastrophilus intestinalis*, *G. nasalis*) and ascarids (*Parascaris equorum*).

(2) It is administered by a stomach tube at a dosage level of 1 fluid ounce per 200 pounds of body weight. The dose is emulsified in a convenient amount of water (½ to 2 pints) at the time of treatment before administration.

(3) The drug should not be given to horses which are severely debilitated, suffering from diarrhea or severe constipation, infectious disease, toxemia or colic until such conditions are corrected with proper therapy.

(4) This drug is a cholinesterase inhibitor. Do not use this drug in animals simultaneously or within a few days before or after treatment with or exposure to cholinesterase-inhibiting drugs, pesticides or chemicals.

(5) Not for use in horses intended for food.

(6) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

§ 520.246 Butorphanol tartrate tablets.

(a) *Specifications.* Each tablet contains 1, 5, or 10 milligrams of butorphanol base activity as butorphanol tartrate.

(b) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(c) *Conditions of use.* The drug is used for the treatment of dogs as follows:

(1) *Amount.* 0.25 milligram of butorphanol base activity per pound of body weight.

(2) *Indications for use.* For the relief of chronic nonproductive cough associated with tracheo-bronchitis, tracheitis, tonsillitis, laryngitis, and pharyngitis associated with inflammatory conditions of the upper respiratory tract.

(3) *Limitations.* For oral use in dogs only. Repeat at intervals of 6 to 12 hours as required. If necessary, increase dose to a maximum of 0.5 milligram per pound of body weight. Treatment should not normally be required for longer than 7 days. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[47 FR 14702, Apr. 6, 1982, as amended at 53 FR 27851, July 25, 1988]

§ 520.260 n-Butyl chloride capsules.

(a)(1) *Specifications.* n-Butyl chloride capsules, veterinary contain 272 milligrams or 816 milligrams of n-butyl chloride in each capsule.

(2) *Sponsor.* See No. 000031 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) It is used for the removal of ascarids (*Toxocara canis* and *Toxascaris leonina*) and hookworms (*Ancylostoma caninum*, *Ancylostoma braziliense*, and *Uncinaria stenocephala*) from dogs and of the ascarid (*Toxocara cati*) and hookworm (*Ancylostoma tubaeforme*) from cats.

(ii)(a) Animals should not be fed for 18 to 24 hours before being given the drug. Puppies and kittens should be wormed at 6 weeks of age. However, if heavily infested, they may be wormed at 4 or 5 weeks of age. Administration of the drug should be followed in ½ to 1 hour with a teaspoonful to a tablespoonful of milk of magnesia or 1 or 2 milk of magnesia tablets. Normal rations may be resumed 4 to 8 hours

after treatment. Puppies and kittens should be given a repeat treatment in a week or 10 days. After that they should be treated every 2 months (or as symptoms reappear) until a year old. When the puppy or kitten is a year old, one treatment every 3 to 6 months is sufficient.

(b) For dogs or cats that have been wormed regularly, treatment every 3 to 6 months will be sufficient. If a dog or cat has not been wormed previously and has the symptoms of large roundworms a dose should be given and repeated in 10 days. Removal of hookworms may require 3 or 4 doses at 10-day intervals.

(c) Puppies, dogs, cats, or kittens weighing 1 to 3 pounds should be given 2 capsules per dose which contain 272 milligrams of *n*-butyl chloride each. Such animals weighing 4 to 5 pounds should be given 3 such capsules. Animals weighing 6 to 7 pounds should be given 4 such capsules and animals weighing 8 to 9 pounds should be given 5 such capsules. Animals weighing 10 to 20 pounds should be given 3 capsules which contain 816 milligrams of *n*-butyl chloride each, animals weighing 20 to 40 pounds should be given 4 such capsules and animals weighing over 40 pounds should be given 5 such capsules with the maximum dosage being 5 capsules, each of which contains 816 milligrams of *n*-butyl chloride.

(iii) A veterinarian should be consulted before using in severely debilitated dogs or cats and also prior to repeated use in cases which present signs of persistent parasitism.

(b)(1) *Specifications.* *n*-Butyl chloride capsules contain 221, 442, 884, or 1,768 milligrams or 4.42 grams of *n*-butyl chloride in each capsule.¹

(2) *Sponsors.* See Nos. 015563 and 023851 in § 510.600(c) of this chapter for 221, 442, 884, or 1,768 milligram or 4.42 gram capsules; No. 000115 or 012983 for 884 or 1,768 milligram or 4.42 gram capsules; and No. 000069 for 221 milligram capsules.

¹These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter.

(3) *Conditions of use.* (i) It is used for the removal of ascarids (*Toxocara canis* and *Toxascaris leonina*) and hookworms (*Ancylostoma caninum*, *Ancylostoma braziliense*, and *Uncinaria stenocephala*) from dogs.¹

(ii)(a) Dogs should not be fed for 18 to 24 hours before being given the drug. Administration of the drug should be followed in ¼ to 1 hour with a mild cathartic. Normal feeding may be resumed 4 to 8 hours after treatment. Animals subject to reinfection may be retreated in 2 weeks.¹

(b) The drug is administered orally to dogs. Capsules containing 221 milligrams of *n*-butyl chloride are administered to dogs weighing under 5 pounds at a dosage level of 1 capsule per 1¼ pound of body weight. Capsules containing 442 milligrams of *n*-butyl chloride are administered to dogs weighing under 5 pounds at a dosage level of 1 capsule per 2½ pounds body weight. Capsules containing 884 milligrams of *n*-butyl chloride are administered to dogs as follows: Weighing under 5 pounds, 1 capsule; weighing 5 to 10 pounds, 2 capsules; weighing 10 to 20 pounds, 3 capsules; weighing 20 to 40 pounds, 4 capsules; over 40 pounds, 5 capsules. Capsules containing 1,768 milligrams of *n*-butyl chloride are administered at a dosage level of 1 capsule per dog weighing 5 to 10 pounds. Capsules containing 4.42 grams of *n*-butyl chloride are administered at a dosage level of 1 capsule per dog weighing 40 pounds or over.¹

(iii) A veterinarian should be consulted before using in severely debilitated dogs.¹

(c)(1) *Specifications.* *n*-Butyl chloride capsules, veterinary contain 884 or 1,768 milligrams or 4.42 grams of *n*-butyl chloride in each capsule.

(2) *Sponsor.* See No. 000115 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) It is used for the removal of ascarids (*Toxocara canis* and *Toxascaris leonina*) and hookworms (*Ancylostoma caninum*, *Ancylostoma braziliense*, and *Uncinaria stenocephala*) from dogs.

(ii)(a) Dogs should not be fed for 18 to 24 hours before being given the drug. Administration of the drug should be followed in ¼ to 1 hour with a mild cathartic. Normal rations may

be resumed 4 to 8 hours after treatment.

(b) The drug is administered orally to dogs. Capsules containing 884 milligrams of *n*-butyl chloride are administered to dogs as follows: weighing under 5 pounds, 1 capsule; weighing 5-10 pounds, 2 capsules; weighing 10-20 pounds, 3 capsules; weighing 20-40 pounds, 4 capsules; over 40 pounds, 5 capsules. Capsules containing 1,768 milligrams of *n*-butyl chloride are administered at a dosage level of 1 capsule per dog to dogs weighing 5-10 pounds and 2 capsules per dog to dogs weighing 20-40 pounds. Capsules containing 4.42 grams of *n*-butyl chloride are administered at dosage level of 1 capsule per dog to dogs weighing 40 pounds or over.

(iii) A veterinarian should be consulted before using in severely debilitated dogs.

[40 FR 13838, Mar. 27, 1975, as amended at 40 FR 39858, Aug. 29, 1975; 44 FR 10059, Feb. 16, 1979]

§ 520.300 Cambendazole oral dosage forms.

[41 FR 1276, Jan. 7, 1976]

§ 520.300a Cambendazole suspension.

(a) *Specifications.* Each fluid ounce contains 0.9 gram of cambendazole.

(b) *Sponsor.* No. 000006 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is used in horses for the control of large strongyles (*Strongylus vulgaris*, *S. edentatus*, *S. equinus*); small strongyles (*Trichonema*, *Poteriostomum*, *Cylicobrachytus*, *Craterostomum*, *Oesophagodontus*); roundworms (*Parascaris*); pinworms (*Oxyuris*); and threadworms (*Strongyloides*).

(2) It is administered by stomach tube or as a drench at a dose of 0.9 gram of cambendazole per 100 pounds of body weight (20 milligrams per kilogram).

(3) For animals maintained on premises where reinfection is likely to occur, re-treatments may be necessary. For most effective results, re-treat in 6 to 8 weeks.

(4) Not for use in horses intended for food.

(5) *Caution:* Do not administer to pregnant mares during first 3 months of pregnancy.

(6) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13838, Mar. 27, 1975. Redesignated at 41 FR 1276, Jan. 7, 1976, and amended at 42 FR 3838, Jan. 21, 1977]

§ 520.300b Cambendazole pellets.

(a) *Specifications.* The drug is in feed pellets containing 5.3 percent cambendazole.

(b) *Sponsor.* No. 000006 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is used in horses for the control of large strongyles (*Strongylus vulgaris*, *S. edentatus*, *S. equinus*); small strongyles (*Trichonema*, *Poteriostomum*, *Cylicobrachytus*, *Craterostomum*, *Oesophagodontus*); roundworms (*Parascaris*); pinworms (*Oxyuris*); and threadworms (*Strongyloides*).

(2) Administer 20 milligrams cambendazole per kilogram body weight (6 ounces per 1,000 pounds) by mixing with normal grain ration given at one feeding. Doses for individual horses should be mixed and fed separately to assure that each horse will consume the correct amount.

(3) For animals maintained on premises where reinfection is likely to occur, re-treatments may be necessary. For most effective results, re-treat in 6 to 8 weeks.

(4) Not for use in horses intended for food.

(5) *Caution:* Do not administer to pregnant mares during first 3 months of pregnancy.

(6) Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

[41 FR 1276, Jan. 7, 1976, as amended at 42 FR 3838, Jan. 21, 1977]

§ 520.300c Cambendazole paste.

(a) *Specifications.* The drug is a paste containing 45 percent cambendazole.

(b) *Sponsor.* No. 000006 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is used in horses for the control of large strongyles (*Strongylus vulgaris*, *S. edenta-*

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tus, *S. equinus*); small strongyles (*Trichonema*, *Poteriostomum*, *Cylicobrachytus*, *Craterostomum*, *Oesophagodontus*); roundworms (*Parascaris*); pinworms (*Oxyuris*); and threadworms (*Strongyloides*).

(2) Administer 20 milligrams cambendazole per kilogram body weight (5 grams per 550 pounds (250 kilograms)) by depositing the paste on the back of the tongue using a dosing gun.

(3) For animals maintained on premises where reinfection is likely to occur, re-treatments may be necessary. For most effective results, re-treat in 6 to 8 weeks.

(4) Not for use in horses intended for food.

(5) Caution: Do not administer to pregnant mares during first 3 months of pregnancy.

(6) Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

[41 FR 1276, Jan. 7, 1976, as amended at 42 FR 3838, Jan. 21, 1977]

§ 520.310 Caramiphen ethanedisulfonate and ammonium chloride tablets.

(a) *Specifications.* Each tablet contains 10 milligrams of caramiphen ethanedisulfonate and 80 milligrams of ammonium chloride.¹

(b) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(c) *Conditions of use in dogs.*—(1) *Amount.* One tablet per 15 to 30 pounds of body weight every 4 to 6 hours.¹

(2) *Indications for use.* For relief of cough.¹

[43 FR 55385, Nov. 28, 1978]

§ 520.314 Cefadroxil tablets.

(a) *Specifications.* 50-, 100-, and 200-milligram tablets for dogs and cats; 1 gram tablet for dogs.

(b) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) For use in dogs as follows:

¹These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(i) *Indications for use.* For the treatment of skin and soft tissue infections including cellulitis, pyoderma, dermatitis, wound infections, and abscesses due to susceptible strains of *Staphylococcus aureus*. For the treatment of genitourinary tract infections (cystitis) due to susceptible strains of *Escherichia coli*, *Proteus mirabilis*, and *Staphylococcus aureus*.

(ii) *Amount.* Ten milligrams per pound of body weight twice daily.

(iii) *Limitations.* The drug is administered orally. For skin and soft tissue infections, treatment should be continued for a minimum of 3 days. For genitourinary tract infections, treatment should be continued for a minimum of 7 days. Continue treatment at least 48 hours after the dog has become afebrile or asymptomatic. If no response is seen after 3 days of treatment, therapy should be discontinued and the case reevaluated. Do not treat for more than 30 days. Safety for use in pregnant bitches and stud dogs has not been determined. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(2) For use in cats as follows:

(i) *Indications for use.* For the treatment of skin and soft tissue infections including abscesses, wound infections, cellulitis, and dermatitis caused by susceptible strains of *Pasteurella multocida*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Streptococcus* spp.

(ii) *Amount.* Ten milligrams per pound of body weight once daily.

(iii) *Limitations.* The drug is administered orally. Continue treatment at least 48 hours after the cat has become afebrile or asymptomatic. If no response is seen after 3 days of treatment, therapy should be discontinued and the case reevaluated. Do not treat for more than 21 days. Safety for use in pregnant cats and breeding male cats has not been determined. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[47 FR 41105, Sept. 17, 1982, as amended at 49 FR 43052, Oct. 26, 1984; 51 FR 4165, Feb. 3, 1986; 52 FR 11989, Apr. 14, 1987; 53 FR 27851, July 25, 1988]

§ 520.315 Cefadroxil powder for oral suspension.

(a) *Specifications.* Cefadroxil powder is reconstituted to form a 50 milligram-per-milliliter aqueous suspension.

(b) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) For use in dogs as follows:

(i) *Indications for use.* For treating genitourinary tract infections (cystitis) caused by susceptible strains of *Escherichia coli*, *Proteus mirabilis*, and *Staphylococcus aureus*; and skin and soft tissue infections including cellulitis, pyoderma, dermatitis, wound infections, and abscesses caused by susceptible strains of *Staphylococcus aureus*.

(ii) *Amount.* 10 milligrams per pound of body weight, twice daily.

(2) For use in cats as follows:

(i) *Indications for use.* For treating skin and soft tissue infections including abscesses, wound infections, cellulitis, and dermatitis caused by susceptible strains of *Pasteurella multocida*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Streptococcus spp.*

(ii) *Amount.* 10 milligrams per pound of body weight, once daily.

(3) *Limitations.* Discard unused portion of reconstituted product after 14 days. Treatment should continue for 48 hours after animal is afebrile or asymptomatic. If no response after 3 days, discontinue treatment and re-evaluate therapy. Not for use in animals raised for food production. Safe use in pregnant or breeding animals has not been established. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[53 FR 27344, July 20, 1988]

§ 520.420 Chlorothiazide tablets and boluses.

(a)(1) *Specifications.* Each tablet contains 0.25 gram of chlorothiazide.

(2) *Sponsor.* See No. 000006 in § 510.600(c) of this chapter.

(3) *Conditions of use.*—(i) *Amount.* Usual dosage is 5 to 10 milligrams per

pound of body weight two or three times daily.¹

(ii) *Indications for use.* For use in dogs for treatment of congestive heart failure and renal edema.¹

(iii) *Limitations.* (a) *Dosage* must be adjusted to meet the changing needs of the individual animal. In mild and responsive cases, it is suggested that a dose of 5 milligrams per pound of body weight be administered two or three times daily. In moderately edematous and moderately responsive animals, a dose of 7.5 to 10 milligrams per pound of body weight may be administered three times daily. Severe conditions may require higher doses. Certain animals may respond adequately to intermittent therapy; in these cases, the drug may be administered either every other day or for 3 to 5 days each week.

(b) Animals should be regularly and carefully observed for early signs of fluid and electrolyte imbalance. Take appropriate countermeasures if this should occur. In some dogs, hypochloremic alkalosis may occur (that is, excretion of chloride in relation to sodium is excessive; the plasma bicarbonate level increases and alkalosis results). Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

(b)(1) *Specifications.* Each bolus contains 2 grams of chlorothiazide.

(2) *Sponsor.* See No. 000006 in § 510.600(c) of this chapter.

(3) *Conditions of use.*—(i) *Amount.* 2 grams once or twice daily for 3 or 4 days.¹

(ii) *Indications for use.* For use in cattle as an aid in reduction of postparturient udder edema.¹

(iii) *Limitations.* Animals should be regularly and carefully observed for early signs of fluid and electrolyte imbalance. Take appropriate countermeasures if this should occur. Milk taken from dairy animals during treatment and for 72 hours (six milkings) after latest treatment must not be used for food. Federal law restricts

¹These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

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this drug to use by or on the order of a licensed veterinarian.¹

[43 FR 39085, Sept. 1, 1978]

§ 520.434 Chlorphenesin carbamate tablets.

(a) *Specifications.* Each tablet contains 400 milligrams of chlorphenesin carbamate.

(b) *Sponsor.* See No. 000009 in § 510.600(c) of this chapter.

(c) *Conditions of use in dogs—(1) Amount.* 50 milligrams per pound of body weight on first day; 25 milligrams per pound of body weight each following day. Divide total daily dose into 2 or 3 equal doses—administer at 12- or 8-hour intervals.

(2) *Indications for use.* For use as an adjunct to therapy of acute inflammatory and traumatic conditions of skeletal muscles. The drug provides relief of the signs of discomfort associated with myositis, muscle sprains, traumatic injuries, stifle injuries—especially when administered before or after surgery—and intervertebral disc syndrome (can be used concurrently with adrenal corticosteroids).

(3) *Limitations.* Not recommended for pregnant animals or those with a known hepatic dysfunction. Periodic liver function studies are recommended for animals on prolonged treatment. If no response is evident within 5 days of the beginning of treatment, the diagnosis should be redetermined and appropriate therapy instituted. Not recommended for use with general anesthetics other than the barbiturates. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[44 FR 16009, Mar. 16, 1979]

§ 520.443 Chlorpromazine hydrochloride.

(a) *Specifications.* The drug is in tablet form with the tablets containing chlorpromazine hydrochloride as the active drug ingredient.

(b) *Sponsor.* See No. 011716 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is administered orally to dogs and cats as

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a tranquilizer, potentiator, and antiemetic with a sedating effect.¹

(2) It is administered orally to dogs and cats at a dosage level of one tablet containing 10 milligrams of chlorpromazine hydrochloride per 7 pounds body weight or at a dosage level of one tablet containing 25 milligrams of chlorpromazine hydrochloride per 17 pounds body weight. It is administered one to four times daily depending upon the size of the dose and the needs of the patient.¹

(3) It is not to be used in conjunction with organophosphates and/or procaine hydrochloride since phenothiazines may potentiate the toxicity of organophosphates and the activity of procaine hydrochloride.¹

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

§ 520.446 Clindamycin hydrochloride capsules.

(a) *Specifications.* Each capsule contains the equivalent of 25, 75, or 150 milligrams of clindamycin as the hydrated hydrochloride salt.

(b) *Sponsor.* No. 000009 in § 510.600(c) of this chapter.

(c) *Conditions of use in dogs—(1) Amount.* Wound infections and abscesses: 2.5 milligrams per pound of body weight every 12 hours for a maximum of 28 days. Osteomyelitis: 5.0 milligrams per pound of body weight every 12 hours for a minimum of 28 days.

(2) *Indications for use.* For use in dogs for treatment of wound infections, abscesses, and osteomyelitis caused by *Staphylococcus aureus*.

(3) *Limitations.* Wound infections and abscesses: Do not use for more than 4 days if no improvement of acute infection is observed. Osteomyelitis: Do not use for more than 28 consecutive days if no improvement is observed. Because of potential adverse gastrointestinal effects, do not administer to rabbits, hamsters, guinea pigs.

¹ These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

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and horses. Use with caution in animals receiving neuromuscular blocking agents, as clindamycin may potentiate their action. Prescribe with caution in atopic animals. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[49 FR 23341, June 6, 1984, as amended at 51 FR 34960, Oct. 1, 1986]

§ 520.447 Clindamycin hydrochloride liquid.

(a) *Specifications.* Each milliliter of 8.64 percent alcoholic solution contains the equivalent of 25 milligrams of clindamycin (as the hydrochloride).

(b) *Sponsor.* No. 000009 in § 510.600(c) of this chapter.

(c) *Condition of use. Dogs—(1)(i) Amount.* 2.5 milligrams per pound of body weight every 12 hours.

(ii) *Indications for use.* For treatment of infected wounds and abscesses caused by *Staphylococcus aureus*.

(iii) *Limitations.* Discontinue use after 3 or 4 days if no improvement of acute infection is observed; do not use for more than 28 consecutive days; use with caution in animals receiving neuromuscular blocking agents as clindamycin may potentiate their action; prescribe with caution in atopic animals; because of potential adverse gastrointestinal effects; do not administer to rabbits, hamsters, guinea pigs, and horses; Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(2)(i) *Amount.* 5 milligrams per pound of body weight every 12 hours.

(ii) *Indications for use.* For treatment of osteomyelitis caused by *Staphylococcus aureus*.

(iii) *Limitations.* Use for a minimum of 28 days; use with caution in animals receiving neuromuscular blocking agents as clindamycin may potentiate their action; prescribe with caution in atopic animals; because of potential adverse gastrointestinal effects, do not administer to rabbits, hamsters, guinea pigs, and horses; Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[50 FR 21239, May 23, 1985, as amended at 51 FR 34960, Oct. 1, 1986]

§ 520.462 Clorsulon drench.

(a) *Specifications.* The drug is a suspension containing 8.5 percent clorsulon (85 milligrams per milliliter).

(b) *Sponsor.* See No. 000006 in § 510.600(c) of this chapter.

(c) *Conditions of use. Cattle—(1) Amount.* One-quarter fluid ounce per 200 pounds of body weight (7 milligrams per kilogram or 3.2 milligrams per pound of body weight).

(2) *Indications for use.* For the treatment of immature and adult liver fluke (*Fasciola hepatica*) infestations in cattle.

(3) *Limitations.* Using dose syringe, deposit drench over back of tongue. Do not treat cattle within 8 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

[50 FR 10221, Mar. 14, 1985]

§ 520.500 Coumaphos crumbles.

(a) *Chemical name.* O,O-Diethyl O-3-chloro-4-methyl-2-oxo-2H-1-benzopyran-7-yl-phosphorothioate.

(b) *Specifications.* Coumaphos Crumbles contain 0.32 percent coumaphos.

(c) *Sponsor.* See No. 000859 in § 510.600(c) of this chapter.

(d) *Special considerations.* Adequate directions and warnings for use must be given and shall include a statement that coumaphos is a cholinesterase inhibitor and that animals being treated with coumaphos should not be exposed during or within a few days before or after treatment with any other cholinesterase inhibiting drugs, insecticides, pesticides, or chemicals.

(e) *Related tolerances.* See 40 CFR 180.189.

(f) *Conditions of use.* It is used as a top dressing on the daily feed ration of cattle for the control of gastrointestinal roundworms (*Haemonchus* spp., *Ostertagia* spp., *Cooperia* spp., *Nematodirus* spp., and *Trichostrongylus* spp.). It is administered at the rate of 1 ounce of coumaphos crumbles per 100 pounds of body weight per day for six consecutive days. Should conditions warrant, treatment should be re-

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peated at 30 day intervals. Not to be fed to cattle less than 3 months old. Not to be fed to sick animals or animals under stress such as those just shipped, dehorned, castrated, or weaned within the previous 3 weeks. Not to be used in conjunction with oral drenches or with feeds containing phenothiazine.

§ 520.530 Cythioate oral liquid.

(a) *Specifications.* Each milliliter contains 15 milligrams of cythioate.

(b) *Sponsor.* See Nos. 000859 and 010042 in § 510.600 of this chapter.

(c) *Special considerations.* Cythioate is a cholinesterase inhibitor. Do not use this product in animals simultaneously with or within a few days before or after treatment with or exposure to cholinesterase-inhibiting drugs, insecticides, pesticides, or chemicals.

(d) *Conditions of use—(1) Amount.* 15 milligrams cythioate per 10 pounds of body weight every third day or twice a week.

(2) *Indications for use.* Dogs, for control of fleas.

(3) *Limitations.* For oral use in dogs only. Do not use in greyhounds or in animals that are pregnant, sick, under stress, or recovering from surgery. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[49 FR 5614, Feb. 14, 1984]

§ 520.531 Cythioate tablets.

(a) *Specifications.* Each tablet contains 30 milligrams of cythioate.

(b) *Sponsor.* See Nos. 000859 and 010042 in § 510.600 of this chapter.

(c) *Special considerations.* Cythioate is a cholinesterase inhibitor. Do not use this product in animals simultaneously with or within a few days before or after treatment with or exposure to cholinesterase-inhibiting drugs, insecticides, pesticides, or chemicals.

(d) *Conditions of use—(1) Amount.* 30 milligrams cythioate per 20 pounds of body weight every third day or twice a week.

(2) *Indications for use.* Dogs, for control of fleas.

(3) *Limitations.* For oral use in dogs only. Do not use in greyhounds or in

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animals that are pregnant, sick, under stress, or recovering from surgery. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[49 FR 5615, Feb. 14, 1984]

§ 520.540 Dexamethasone oral dosage forms.

§ 520.540a Dexamethasone powder.

(a) *Specifications.* Dexamethasone powder is packaged in packets containing 10 milligrams of dexamethasone.

(b) *Sponsor.* See No. 000061 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) Dexamethasone powder is indicated in cases where cattle and horses require additional steroid therapy following its parenteral administration. The drug is used as supportive therapy for management or inflammatory conditions such as acute arthritic lameness, and for various stress conditions where corticosteroids are required while the animal is being treated for a specific condition.

(2) The drug is administered at a dosage level of 5 to 10 milligrams per animal the first day then 5 milligrams per day as required by drench or by sprinkling on a small amount of feed.

(3) Clinical and experimental data have demonstrated that corticosteroids administered orally or parenterally to animals may induce the first stage of parturition when administered during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13838, Mar. 27, 1975; 41 FR 9149, Mar. 3, 1976; 52 FR 7832, Mar. 13, 1987]

§ 520.540b Dexamethasone tablets and boluses.

(a)(1) *Specifications.* Each bolus is half-scored and contains 10 milligrams of dexamethasone.

(2) *Sponsor.* See No. 000061 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (1) Dexamethasone bolus is indicated in cases where cattle and horses require additional

steroid therapy following its parenteral administration. The drug may be used as supportive therapy for management of inflammatory conditions such as acute arthritic lamenesses, and for various stress conditions where corticosteroids are required while the animal is being treated for a specific condition.

(ii) Administered orally, 5 to 10 milligrams for the first day, then 5 milligrams per day as required.

(iii) Do not use in viral infections during the viremic stage. With bacterial infections, appropriate antibacterial therapy should be used.

(iv) Do not use in animals with chronic nephritis and hypercorticalism (Cushingoid syndrome), except for emergency therapy.

(v) Clinical and experimental data have demonstrated that corticosteroids administered orally or by injection to animals may induce the first stage of parturition when administered during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis.

(vi) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(b)(1) *Specifications.* Each tablet contains 0.25 milligram of dexamethasone.¹

(2) *Sponsors.* See Nos. 000061 and 053617 in § 510.600(c) of this chapter.

(3) *Conditions of use—(i) Amount.* Dogs: Administer orally at 0.25 to 1.25 milligrams per day for up to 7 days. Cats: 0.125 to 0.5 milligram per day for up to 7 days.¹

(ii) *Indications for use.* In treatment of dogs and cats as an anti-inflammatory agent.¹

(iii) *Limitations.* (a) Clinical and experimental data have demonstrated that corticosteroids administered orally or by injection to animals may induce the first stage of parturition when administered during the last trimester of pregnancy; and they may precipitate premature parturition fol-

lowed by dystocia, fetal death, retained placenta, and metritis.

(b) Do not use in viral infections. Anti-inflammatory action of corticosteroids may mask signs of infections. Do not use in animals with tuberculosis, chronic nephritis, Cushingoid syndrome, or peptic ulcers, except for emergency therapy.¹

(c) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

[40 FR 26273, June 23, 1975, as amended at 44 FR 7130, Feb. 6, 1979; 50 FR 49372, Dec. 2, 1985; 52 FR 7832, Mar. 13, 1987]

§ 520.540c Dexamethasone chewable tablets.

(a) *Specifications.* Each half-scored tablet contains 0.25 milligram of dexamethasone.¹

(b) *Sponsor.* See No. 000029 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* 0.25 to 1.25 milligrams per day.¹

(2) *Indications for use.* Supportive therapy in nonspecific dermatosis and inflammatory conditions in dogs.¹

(3) *Limitations.* (i) Administer by free-choice feeding or crumble over food. Administer 0.25 to 1.25 milligrams daily in single or two divided doses until response is noted or 7 days have elapsed. When response is attained, dosage should be gradually reduced by 0.125 milligram per day until maintenance level is achieved.

(ii) Clinical and experimental data have demonstrated that corticosteroids administered orally or parenterally to animals may induce the first stage of parturition when administered during the last trimester of pregnancy; and they may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis.

(iii) Do not use in viral infections. Anti-inflammatory action of corticosteroids may mask signs of infection. Do not use in animals with tuberculosis, chronic nephritis, Cushingoid syndrome, or peptic ulcers, except for emergency therapy.¹

(iv) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[44 FR 7130, Feb. 6, 1979]

¹ These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter.

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§ 520.550 Dextrose/glycine/electrolyte.

(a) *Specifications.* The product is distributed in packets each of which contains the following ingredients: sodium chloride 8.82 grams, potassium phosphate 4.20 grams, citric acid anhydrous 0.5 gram, potassium citrate 0.12 gram, aminoacetic acid (glycine) 6.36 grams, and dextrose 44.0 grams.

(b) *Sponsor.* See No. 000029 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) Dextrose/glycine/electrolyte is indicated for use in the control of dehydration associated with diarrhea (scours) in calves. It is used as an early treatment at the first signs of scouring. It may also be used as followup treatment following intravenous fluid therapy.

(2) Dissolve each packet in two quarts of warm water and administer to each calf as follows:

(i) *Scouring and/or dehydrated calves.* Feed 2 quarts of solution, twice daily for 2 days (four feedings). No milk or milk replacer should be fed during this period. For the next four feedings (days 3 and 4), use 1 quart of solution together with 1 quart of milk replacer. Thereafter, feed as normal.

(ii) *Newly purchased calves.* Feed 2 quarts of solution instead of milk as the first feed upon arrival. For the next scheduled feeding, use 1 quart of solution mixed together with 1 quart of milk or milk replacer. Thereafter, feed as normal.

(3) The product should not be used in animals with severe dehydration (down, comatose, or in a state of shock). Such animals need intravenous therapy. Oral therapy in these cases is too slow. Animals which cannot drink after initial intravenous therapy may need to be dosed with a stomach tube or esophageal tube. Adequate colostrum intake during the first 12 hours is essential for healthy, vigorous calves. Antibacterial therapy is often indicated in bacterial scours due to *E. coli* and/or *Salmonella*. The product does not contain antibacterial agents. A veterinarian should be consulted in severely scouring calves or cases requiring antibacterial therapy. The product is not nutritionally complete if administered by itself for long periods of time. It should not be administered beyond the recommended treat-

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ment period without the addition of milk or milk replacer.

[48 FR 38606, Aug. 25, 1983]

§ 520.563 Diatrizoate meglumine and diatrizoate sodium oral solution.

(a) *Specifications.* Diatrizoate meglumine oral solution is a water soluble radiopaque medium containing 66 percent diatrizoate meglumine and 10 percent diatrizoate sodium.

(b) *Sponsor.* See No. 053501 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is indicated for radiography of the gastrointestinal tract in dogs and cats.

(2) It is administered orally at a dosage level of 0.5 to 1.0 milliliter per pound of body weight by gavage or stomach tube. It is administered rectally at a dosage level of 0.5 to 1.0 milliliter per pound of body weight diluted with 1 part of the drug to 5 parts of water.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[44 FR 12993, Mar. 9, 1979, as amended at 50 FR 41489, Oct. 11, 1985]

§ 520.580 Dichlorophene and toluene capsules.

(a) *Specifications.* Each soft gelatin capsule contains 50 milligrams of dichlorophene and 60 milligrams of toluene or multiples thereof.¹

(b) *Sponsor.* (1) For single dose only, see 000010, 000115, 000842, 000856, 010888, 011536, 011614, 015563, 017135, 023851, 049968, 050906, and 055025 in § 510.600(c) of this chapter.

(2) For single and multiple dose, see 000859, 011716, 038782, and 054273 in § 510.600(c) of this chapter.

(c) *Required statement.* Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism, and before administering to weak or debilitated animals.

(d) *Conditions of use—(1) Amount.* (i) Single dose of 100 milligrams of di-

¹ These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

chlorophene and 120 milligrams of p-phenylene per pound of body weight.¹

(ii) Divided dose of 100 milligrams of chlorophene and 120 milligrams of p-phenylene per 5 pounds of body weight (20 and 24 milligrams per pound) daily for 6 days.¹

(2) *Indications for use.* It is used for the removal of ascarids (*Toxocara canis* and *Toxascaris leonina*) and hookworms (*Ancylostoma caninum* and *Uncinaria stenocephala*) and as aid in removing tapeworms (*Taenia stiformis*, *Dipylidium caninum*, and *Chinococcus granulatus*) from dogs and cats.¹

(3) *Limitations.* Withhold solid foods and milk for at least 12 hours prior to medication and for 4 hours afterward. Repeat treatment in 2 to 4 weeks in animals subject to reinfection.¹

FR 10332, Feb. 15, 1980, as amended at FR 17482, Apr. 23, 1982; 52 FR 39512, Oct. 22, 1987; 53 FR 21993, June 13, 1988; 53 FR 40727, Oct. 18, 1988; 54 FR 6659, Feb. 14, 1989.

§ 520.581 Dichlorophene tablets.

(a) *Specifications.* Each tablet contains 1 gram of dichlorophene.

(b) *Sponsor.* See 023851 in § 520.600(c) of this chapter.

(c) *Required statement.* Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism, and before administering to weak or debilitated animals.

(d) *Conditions of use—Dogs—(1) Amount.* Single dose of 1 tablet (1 gram of dichlorophene) for each 10 pounds of body weight.

(2) *Indications for use.* It is used as aid in the removal of tapeworms (*Taenia stiformis* and *Dipylidium caninum*).

(3) *Limitations.* Withhold solid foods and milk for at least 12 hours prior to medication and for 4 hours afterward.

FR 10333, Feb. 15, 1980

§ 520.600 Dichlorvos.

(a) *Chemical name.* 2,2-Dichlorovinyl dimethyl phosphate.

(b) [Reserved]

(c) *Sponsor.* See No. 054273 in § 520.600(c) of this chapter.

(d) *Related tolerances.* See § 556.180 of this chapter.

(e) *Conditions of use in swine.* (1) It is recommended for the removal and control of sexually mature (adult), sexually immature and/or 4th stage larvae of the whipworm (*Trichuris suis*), nodular worms (*Oesophagostomum* spp.), large round-worm (*Ascaris suum*), and the mature thick stomach worm (*Ascarops strongylina*) occurring in the lumen of the gastrointestinal tract of pigs, boars, and open or bred gilts and sows.

(2) The preparation should be added to the indicated amount of feed as set forth in paragraph (e)(2) of this section and administered shortly after mixing, as follows:

Weight of animal in pounds	Pounds of feed to be mixed with each 0.08 ounce of dichlorvos	Pounds of mixed feed to be administered to each pig as a single treatment	Number of pigs to be treated per 0.08 ounce of dichlorvos
20-30.....	4	0.33	12
31-40.....	5	0.56	9
41-60.....	6	1.00	6
61-80.....	5	1.00	5
81-100.....	4	1.00	4
Adult Gilts, Sows, and Boars.....	16	4.00	4

(3) Do not use this product on animals either simultaneously or within a few days before or after treatment with or exposure to cholinesterase inhibiting drugs, pesticides, or chemicals. The preparation should be mixed thoroughly with the feed on a clean, impervious surface. Do not allow swine access to feed other than that containing the preparation until treatment is complete. Do not treat pigs with signs of scours until these signs subside or are alleviated by proper medication. Resume normal feeding schedule afterwards. Swine may be retreated in 4 to 5 weeks.

(f) *Conditions of use in dogs.* (1) For removal of *Toxocara canis* and *Toxascaris leonina* (roundworms), *Ancylostoma caninum* and *Uncinaria stenocephala* (hookworms), and *Trichuris vulpis* (whipworm) residing in the lumen of the gastrointestinal tract.

(2) The drug is in capsule form for direct administration and in pellet

form for administration in about one-third of the regular canned dog food ration or in ground meat. Dogs may be treated with any combination of capsules and/or pellets so that the animal receives a single dose equaling 12 to 15 milligrams of the active ingredient per pound of body weight. One-half of the single recommended dosage may be given, and the other half may be administered 8 to 24 hours later. This split dosage schedule should be used in animals which are very old, heavily parasitized, anemic, or otherwise debilitated. The drug should not be used in dogs weighing less than 2 pounds.

(3) In some dogs, efficacy against *Trichurias vulpis* (whipworm) may be erratic. Dogs that do not develop a negative stool for *Trichuris vulpis* ova 10 to 14 days following initial treatment should be re-treated. If a negative stool is not obtained in 10 to 14 days following re-treatment, alternate means of therapy should be considered.

(4) Do not use in dogs infected with *Dirofilaria immitis*.

(5) Do not use with other anthelmintics, taeniocides, antifilarial agents, muscle relaxants, or tranquilizers.

(6) The drug is a cholinesterase inhibitor. Not for use simultaneously or within a few days before or after treatment with or exposure to cholinesterase-inhibiting drugs, pesticides, or chemicals.

(7) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(g) *Conditions of use in horses when administered in grain.* (1) It is recommended for the removal and control of bots (*Gastrophilus intestinalis*, *G. nasalis*), large strongyles (*Strongylus vulgaris*, *S. equinus*, *S. edentatus*), small strongyles (of the genera *Cyathostomum*, *Cylicocercus*, *Cylicocyclus*, *Cylicodontophorus*, *Triodontophorus*, *Poteriostomum*, *Gyalocephalus*), pinworms (*Oxyuris equi*), and large roundworm (*Parascaris equorum*) in horses including ponies and mules. Not for use in foals (sucklings and young weanlings).

(2) For a satisfactory diagnosis, a microscopic fecal examination should be performed by a veterinarian or a diagnostic laboratory prior to worming.

(3) It is administered in the grain portion of the ration at a dosage of 14.2 milligrams to 18.5 milligrams per pound of body weight as a single dose. It may be administered at one-half of the single recommended dosage and repeated 8 to 12 hours later in the treatment of very aged, emaciated or debilitated subjects or those reluctant to consume medicated feed. In suspected cases of severe ascarid infection sufficient to cause concern over mechanical blockage of the intestinal tract, the split dosage should be utilized.

(4) Do not use in horses which are severely debilitated, suffering from diarrhea or severe constipation, infectious disease, toxemia or colic. Do not administer in conjunction with or within 1 week of administration of muscle relaxant drugs, phenothiazine derived tranquilizers or central nervous system depressant drugs. Horses should not be subjected to insecticide treatment for 5 days prior to or after treating with the drug. Do not administer to horses afflicted with chronic alveolar emphysema (heaves) or related respiratory conditions. The product is a cholinesterase inhibitor and should not be used simultaneously or within a few days before or after treatment with or exposure to cholinesterase inhibiting drugs, pesticides or chemicals.

(5) Do not use in animals other than horses, ponies, and mules. Do not use in horses, ponies, and mules intended for food purposes. Do not allow fowl access to feed containing this preparation or to fecal excrement from treated animals.

(h) *Conditions of use in horses when administered orally by syringe.* (1) It is recommended for the removal and control of first, second, and third instar bots (*Gastrophilus intestinalis* and *G. nasalis*), sexually mature and sexually immature (4th stage) ascarids (*Parascaris equorum*) in horses and foals.

(2) The product is in the form of a gel which is administered directly from a syringe onto the horse's tongue. The product is administered at a dosage level of 20 milligrams of dichlorvos per kilogram of body weight for the removal of bots and ascarids. The

same dosage level is repeated every 21 to 28 days for the control of bots and ascarids. For the control of bots only, the repeat dosage is 10 milligrams per kilogram of body weight every 21 to 28 days during bot fly season.

(3) Do not use this product in animals simultaneously or within a few days before or after treatment with or exposure to cholinesterase-inhibiting drugs, pesticides or chemicals. Do not administer in conjunction with or within 1 week of administration of muscle-relaxant drugs, phenothiazine derived tranquilizers, or central nervous system depressants.

(4) Do not use in horses which are severely debilitated or suffering from diarrhea or severe constipation, infectious disease, toxemia, or colic. Do not administer to horses affected with chronic alveolar emphysema (heaves) or other respiratory conditions.

(5) Do not use in horses intended for food purposes.

(6) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(i) *Conditions of use in cats and puppies.* (1) It is indicated for the removal and control of roundworms *Toxocara canis*, *Toxocara cati*, *Toxascaris leonina* and hookworms (*Ancylostoma caninum*, *Ancylostoma tubaeforme*, *Uncinaria stenocephala*) occurring in the intestinal tracts of cats and puppies.

(2) The drug is in tablet form and is administered orally at a dosage level of 5 mg of the active ingredient per pound of body weight.

(3) Do not administer to puppies or cats showing signs of constipation, mechanical blockage of the intestinal tract, impaired liver function, or to animals recently exposed to or showing signs of infectious disease. The drug is a cholinesterase inhibitor and should not be used simultaneously or within a few days before or after treatment with or exposure to cholinesterase-inhibiting drugs, pesticides, or chemicals.

(4) Do not use in animals under 10 days of age or under 1 pound of body weight.

(5) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13838, Mar. 27, 1975, as amended at 48 FR 40704, Sept. 9, 1983; 51 FR 28546, Aug. 8, 1986]

§ 520.620 Diethylcarbamazine oral dosage forms.

§ 520.620a Diethylcarbamazine.

(a) *Chemical name.* *N,N*-Diethyl-4-methyl-1-piperazine carboxamide.

(b) *Specifications.* Each pound of the drug contains 30 grams of diethylcarbamazine (as base).

(c) *Sponsor.* See No. 000859 in § 510.600(c) of this chapter.

(d) *Conditions of use.* (1) It is administered to dogs to aid in the continual control of large roundworms (*Toxocara canis*) and to aid in the prevention of heartworm disease (*Dirofilaria immitis*). In those areas where roundworms are suspected or known to be a problem, it is added to the daily diet. In those areas where heartworms are endemic, it is added to the daily diet at the beginning of the mosquito activity and treatment is continued throughout the mosquito season and for approximately 1 month thereafter.

(2) It is administered daily in meal or moist feeds as follows:

Weight of animal in pounds	Recommended amount per day	Dosage in milligrams
20.....	¼ level teaspoonful.....	32
50.....	½ level teaspoonful.....	70
100.....	1 level teaspoonful.....	149

(3) Dogs with established heartworm infections should not receive diethylcarbamazine until they have been converted to a negative status.

(4) For use only by or on the order of a licensed veterinarian.

[46 FR 1260, Jan. 6, 1981, as amended at 47 FR 14150, Apr. 2, 1982]

§ 520.620b Diethylcarbamazine chewable tablets.

(a) *Specifications.* Each chewable tablet contains diethylcarbamazine equivalent to 60 or 180 milligrams of diethylcarbamazine citrate adsorbed on an inert resin base.

(b) *Sponsor.* See No. 000859 in § 510.600 of this chapter.

(c) *Conditions of use in dogs*—(1) *Amount.* 3 milligrams per pound of body weight daily.

(2) *Indications.* As an aid in the control of ascarid infections (*Toxocara canis*) and for the prevention of heartworm disease (*Dirofilaria immitis*) in dogs.

(3) *Limitations.* Do not use in dogs that may be harboring heartworms. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[46 FR 1260, Jan. 6, 1981, as amended at 46 FR 51383, Oct. 20, 1981; 47 FR 14150, Apr. 2, 1982]

§ 520.622 Diethylcarbamazine citrate oral dosage forms.

§ 520.622a Diethylcarbamazine citrate tablets.

(a) *Sponsors.* (1) See 000859 and 015579 in § 510.600(c) of this chapter for use of 50, 200, and 400 milligram tablets for prevention of heartworm disease in dogs and as an aid in the treatment of ascarid infections in dogs and cats.

(2) See 053501 in § 510.600(c) of this chapter for use of 100, 200, and 300 milligram tablets for prevention of heartworm disease in dogs and as an aid in the treatment of ascarid infections in dogs.

(3) See 053617 in § 510.600(c) of this chapter for use of 50, 100, 200, 300, or 400 milligram tablets for prevention of heartworm disease in dogs, as an aid in the control of ascarid infections in dogs, and as an aid in the treatment of ascarid infections in dogs and cats.

(4) See 017030 in § 510.600(c) of this chapter for use of 50, 100, 200, 300, and 400 milligram tablets for prevention of heartworm disease in dogs and as an aid in the treatment of ascarid infections in dogs and cats.

(5) See 000081 in § 510.600(c) of this chapter for use of 60, 120, or 180 milligram tablets for prevention of heartworm disease in dogs, as an aid in the control of ascarid infections in dogs, and as an aid in the treatment of ascarid infections in dogs and cats.

(6) See No. 054273 in § 510.600(c) of this chapter for use of 50, 100, 200, 300, or 400 milligram tablets for prevention of heartworm disease in dogs,

as an aid in the control of ascarid infections in dogs, and as an aid in the treatment of ascarid infections in dogs and cats.

(b) *Conditions of use*—(1) *Dosage/indications for use.* (i) Three milligrams per pound of body weight daily for prevention of heartworm disease (*Dirofilaria immitis*) in dogs.

(ii) Three milligrams per pound of body weight daily as an aid in the control of ascarid infections (*Toxocara canis*) in dogs.

(iii) Twenty-five to 50 milligrams per pound of body weight as an aid in the treatment of ascarid infections in dogs (*Toxocara canis*) and cats (*Toxascaris leonina*).

(2) *Limitations.* Administer orally either pulverized and given in feed or water or directly by mouth. For the treatment of ascarid infections, repeat in 10 to 20 days to remove immature worms that may enter the intestine from the lungs after the first dose. Do not treat dogs with established heartworm infections until they have been converted to a negative status by the use of adulticidal and microfilaricidal drugs. Inadvertent administration to heartworm-infected dogs may cause adverse reactions because of pulmonary occlusion. Overdosage may cause emesis. For prevention of heartworm disease in heartworm-endemic areas, administration of the drug should start at the beginning of mosquito activity and be continued daily throughout the mosquito season and for approximately a month thereafter. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[46 FR 23230, Apr. 24, 1981, as amended at 46 FR 41038, Aug. 14, 1981; 46 FR 46315, Sept. 18, 1981; 46 FR 61653, Dec. 18, 1981; 47 FR 10805, Mar. 12, 1982; 47 FR 14150, Apr. 2, 1982; 50 FR 41489, Oct. 11, 1985; 50 FR 49372, Dec. 2, 1985; 53 FR 40056, Oct. 13, 1988; 53 FR 40727, Oct. 18, 1988]

§ 520.622b Diethylcarbamazine citrate syrup.

(a)(1) *Specifications.* Each milliliter of syrup contains 60 milligrams of diethylcarbamazine citrate.

(2) *Sponsor.* See Nos. 021188 and 053501 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) The drug is indicated for use in dogs for the pre-

vention of infection with *Dirofilaria immitis* and *T. canis* and *T. leonina*. It is also indicated for treatment of ascarid infections of *T. canis* and *T. leonina* in dogs and *T. cati* in cats.

(ii) For prevention of heartworm and ascarid infections in dogs, the drug may be added to the daily diet at a dosage rate of 3.0 milligrams per pound of body weight per day or given directly by mouth at the same dosage rate. For treatment of ascarid infections in dogs and cats, the drug is administered at a dosage level of 25 to 50 milligrams per pound of body weight preferably administered immediately after feeding.

(iii) Older dogs should be proven negative for the presence of *Dirofilaria immitis* infection before administration of the drug. Those with proven infection of *Dirofilaria immitis* should be rendered negative using adulticidal and microfilaricidal drugs before administration of this drug.

(iv) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(b)(1) *Specifications*. Each milliliter of syrup contains 60 milligrams of diethylcarbazine citrate.

(2) *Sponsors*. (i) See No. 000859 in § 510.600(c) of this chapter for use as a paragraph (b)(3)(ii) (a) and (b) of this section.

(ii) See No. 017030 for use as in paragraphs (b)(3)(ii) (a) and (c) of this section.

(3) *Conditions of use*—(i) *Amount*. 3 milligrams per pound of body weight per day for prevention of heartworm disease and as an aid in control of large roundworms; 25 to 50 milligrams per pound of body weight as an aid in treatment of ascarid infections.

(ii) *Indications for use*. (a) For prevention of heartworm disease (*Dirofilaria immitis*) in dogs.

(b) As an aid in control of large roundworms (*T. canis*) in dogs.

(c) As an aid in treatment of ascarid infections in dogs (*T. canis*) and cats (*T. canis* and *T. leonina*).

(iii) *Limitations*. The drug may be placed on the daily ration or given directly by mouth. For treatment of ascarid infections, a repeat dose should be given in 10 to 20 days to remove immature worms which may enter the

intestine from the lungs after the first dose. Older dogs should be proven negative for presence of *Dirofilaria immitis* infections before administering the drug. Dogs with established heartworm infections should not receive the drug until they have been converted to a negative status by the use of adulticidal and microfilaricidal drugs. Inadvertent administration to heartworm-infected dogs may cause adverse reactions due to pulmonary occlusion. Overdosage may cause emesis. For prevention of heartworm disease in heartworm-endemic areas, administration of the drug should start 1 month before the mosquito season and be continued daily throughout the mosquito season and for 2 months thereafter. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(c)(1) *Specifications*. Each milliliter of syrup contains 60 milligrams of diethylcarbazine citrate.

(2) *Sponsor*. See No. 054273 in § 510.600(c) of this chapter.

(3) *Conditions of use*. (i) The drug is used in dogs between 4 weeks and 8 months of age for the removal of ascarids (*Toxocara canis*) and in animals over 4 weeks of age for the prevention of heartworm disease (*Dirofilaria immitis*).

(ii) The drug is administered (a) for removal of ascarids at a dosage of 50 milligrams per pound of body weight divided into two equal doses and administered 8 to 12 hours apart (morning and night), orally or mixed with either dry or wet food, and (b) for prevention of heartworm disease at a dosage of 3 milligrams per pound of body weight daily, orally or in food, in heartworm endemic areas, from the beginning of mosquito activity, during the mosquito season, and for 2 months following the end thereof.

(iii) Dogs older than 8 months of age may be infected with *Dirofilaria immitis*. Use of the drug is contraindicated in dogs with active *D. immitis* infections.

(iv) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13838, Mar. 27, 1975, as amended at 41 FR 28265, July 9, 1976; 44 FR 3967, Jan. 19, 1979; 47 FR 14150, Apr. 2, 1982; 47 FR

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35186, Aug. 13, 1982; 49 FR 33997, Aug. 28, 1984; 50 FR 41489, Oct. 11, 1985; 53 FR 47027, Oct. 18, 1988]

§ 520.622c Diethylcarbamazine citrate chewable tablets.

(a) *Specifications.* Each chewable tablet contains 30, 45, 60, 120, 150, or 180 milligrams of diethylcarbamazine citrate.

(b) *Sponsors.* See drug listing nos. in § 510.600(c) of this chapter for identification of sponsors as follows:

(1) For 015579, use of 30 or 120 milligram tablets as in paragraph (c)(2)(i) of this section.

(2) For 011519, use of 60, 120, or 180 milligram tablets as in paragraph (c)(2)(ii) of this section.

(3) For 032998, use of 45 or 150 milligram tablets as in paragraph (c)(2)(iii) of this section.

(4) For 053617, use of 60-, 120-, or 180-milligram tablets as in paragraph (c)(2)(i) of this section.

(5) For 017220, use of 60-milligram tablets as in paragraph (c)(2)(i) of this section.

(6) For 054273, use of 30, 60, 120, or 180 milligram tablets as in paragraph (c)(2)(i) of this section.

(7) For 000029 use of 60, 120, or 180 milligram tablets as in paragraph (c)(2)(ii) of this section.

(c) *Conditions of use—(1) Amount.* 3 milligrams per pound of body weight per day for prevention of heartworm disease and control of ascarids; 25 to 50 milligrams per pound of body weight as an aid in treatment of ascarid infections.

(2) *Indications for use.* (i) For prevention of heartworm disease (*Dirofilaria immitis*) in dogs; as an aid in control of ascarids (*Toxocara canis*) in dogs; as an aid in treatment of ascarid (*Toxocara canis* and *Toxascaris leonina*) infections in dogs and cats.

(ii) For prevention of infection with *Dirofilaria immitis* (heartworm disease) in dogs; as an aid in treatment of ascarid (*Toxocara canis* and *Toxascaris leonina*) infections in dogs.

(iii) For prevention of heartworm disease (*Dirofilaria immitis*) in dogs.

(3) *Limitations.* Tablets are administered orally or pulverized and given in the feed. For treatment of ascarid infections, a repeat dose should be given in 10 to 20 days to remove immature

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worms which may enter the intestine from the lungs after the first dose. Dogs with established heartworm infections should not receive the drug until they have been converted to a negative status by the use of adulticidal and microfilaricidal drugs. Inadvertent administration to heartworm-infected dogs may cause adverse reactions due to pulmonary occlusion. Overdosage may cause emesis. For prevention of heartworm disease in heartworm-endemic areas, administration of the drug should start at the beginning of mosquito activity and be continued daily throughout the mosquito season and for approximately a month thereafter. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[43 FR 6941, Feb. 17, 1978, as amended at 44 FR 16010, Mar. 16, 1979; 45 FR 61286, Sept. 16, 1980; 46 FR 25609, May 8, 1981; 47 FR 8348, Feb. 26, 1982; 47 FR 22516, May 25, 1982; 48 FR 9247, Mar. 4, 1983; 50 FR 49372, Dec. 2, 1985; 53 FR 40056, Oct. 13, 1988; 53 FR 40727, Oct. 18, 1988]

§ 520.622d Diethylcarbamazine citrate capsules.

(a)(1) *Specifications.* Each capsule contains either 12.5, 50, 200, or 400 milligrams of diethylcarbamazine citrate.

(2) *Sponsor.* See 011014 in § 510.600(c) of this chapter.

(3) *Conditions of use—(1) Amount/indications for use.* 3 milligrams per pound of body weight daily for prevention of heartworm disease (*Dirofilaria immitis*) in dogs; 25 to 50 milligrams per pound of body weight in a single dose as an aid in the treatment of ascarid infections in dogs (*Toxocara canis* and *Toxascaris leonina*).

(ii) *Limitations.* Administer orally directly or added to the daily ration. For ascarid infections, repeat treatment in 10 to 20 days to remove immature worms that may enter the intestine from the lungs after the first dose. Do not treat dogs with established heartworm infections until they have been converted to a negative status by the use of adulticidal and microfilaricidal drugs. Inadvertent administration to heartworm-infected dogs may cause adverse reactions due to pulmonary occlusion or shock.

Overdosage may cause emesis. For prevention of heartworm disease in heartworm-endemic areas, administration of the drug should begin 1 month before and continue 2 months after the mosquito season. Dogs receiving prophylactic therapy should be examined every 6 months for the presence of microfilariae. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(b)(1) *Specifications.* Each capsule contains either 12.5, 50, 200, or 400 milligrams of diethylcarbamazine citrate.

(2) *Sponsor.* See 023851 in 510.600(c) of this chapter.

(3) *Conditions of use—(i) Amount/indications for use.* 3 milligrams per pound of body weight daily for prevention of heartworm disease (*Dirofilaria immitis*) in dogs.

(ii) *Limitations.* Capsules may be administered to the dog directly or added to the daily ration. For oral administration only. Do not treat dogs with established heartworm infections until they have been converted to a negative status by the use of adulticidal and microfilaricidal drugs. Inadvertent administration to heartworm infected dogs may cause adverse reactions due to pulmonary occlusion or shock. For prevention of heartworm disease in heartworm-endemic areas, administration of the drug should begin 1 month before and continue 2 months after the mosquito season. Dogs receiving prophylactic therapy should be examined every 6 months for the presence of microfilariae. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

7 FR 26377, June 18, 1982, as amended at 49 FR 48979, Oct. 17, 1983; 49 FR 5099, Feb. 1, 1984]

520.623 Diethylcarbamazine citrate, oxibendazole chewable tablets.

(a) *Specifications.* Each tablet contains either 60, 120, or 180 milligrams of diethylcarbamazine citrate with 45, 90, or 136 milligrams of oxibendazole, respectively.

(b) *Sponsor.* See 011519 in 510.600(c) of this chapter.

(c) *Conditions of use in dogs—(1) Amount.* Administer orally to dogs at a dosage level of 6.6 milligrams of dieth-

ylcarbamazine citrate per kilogram of body weight (3 milligrams per pound of body weight) and 5.0 milligrams of oxibendazole per kilogram of body weight (2.27 milligrams per pound of body weight).

(2) *Indications for use.* For prevention of infection with *Dirofilaria immitis* (heartworm disease) and *Ancylostoma caninum* (hookworm infection) and for removal and control of *Trichuris vulpis* (whipworm infection) and mature and immature stages of intestinal *Toxocara canis* (ascarid infection).

(3) *Limitations.* Orally administer daily during heartworm season. For free-choice feeding or broken and placed on or mixed with feed. Do not use in dogs that may harbor adult heartworms. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[50 FR 28768, July 16, 1985, as amended at 53 FR 45759, Nov. 14, 1988; 54 FR 3776, Jan. 26, 1989; 54 FR 6804, Feb. 14, 1989]

§ 520.704 Diphenylhydantoin sodium capsules.

(a) *Specifications.* Diphenylhydantoin sodium capsules conform to U.S.P. XVIII requirements.

(b) *Sponsor.* See No. 000071 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is indicated for use in the control of epileptiform convulsions in dogs.¹

(2) An initial dose of from 4 to 8 milligrams per pound of body weight in divided doses is suggested with the dose then gradually increased or decreased to the daily minimum amount necessary to maintain control.¹

(3) Since control with the drug requires several days, the transition from other anticonvulsants to this drug should be gradual. Sudden withdrawal of other anticonvulsants, including phenobarbital, should be avoided in order to exercise proper control of the convulsions.¹

¹These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

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(4) For use only by or on the order of a licensed veterinarian.¹

§ 520.763 Dithiazanine iodide oral dosage forms.

§ 520.763a Dithiazanine iodide tablets.

(a) *Chemical name.* 3-Ethyl-2-[5-(3-ethyl-2-benzothiazolinyldene)-1,3-pentadienyl]-benzothiazolium iodide.

(b) *Specifications.* Dithiazanine iodide tablets contain 10 milligrams, 50 milligrams, 100 milligrams, or 200 milligrams of dithiazanine iodide in each tablet.

(c) *Sponsor.* See No. 054273 in § 510.600(c) of this chapter.

(d) *Conditions of use.* (1) The tablets are administered orally to dogs immediately after feeding using the following dosage schedule for various parasite infestations:

	Milligrams per pound of body weight	Length of treatment—days
Large roundworms (<i>Toxocara canis</i> , <i>Toxascaris leonina</i>).....	10	3-5
Hookworms (<i>Ancylostoma caninum</i> , <i>Uncinaria stenocephala</i>).....	10	7
Whipworms (<i>Trichuris vulpis</i>).....	10	7
Strongyloides (<i>Strongyloides canis</i> , <i>Strongyloides stercoralis</i>).....	10	10-12
Heartworm microfilariae (<i>Dirofilaria immitis</i>).....	3-5	7-10

Note: Treatment with dithiazanine iodide for heartworm microfilariae should follow 6 weeks after therapy for adult worms.

(2) The drug is contraindicated in animals sensitive to dithiazanine iodide and should be used cautiously, if at all, in dogs with reduced renal function.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(e) Use for treating dogs for large roundworms, hookworms, whipworms, and strongyloides as provided for in this section has been NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

[40 FR 13838, Mar. 27, 1975, as amended at 47 FR 51564, Nov. 16, 1982; 48 FR 32342, July 15, 1983; 53 FR 40727, Oct. 18, 1988]

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§ 520.763b Dithiazanine iodide powder.

(a) *Chemical name.* 3-Ethyl-2-[5-(3-ethyl-2-benzothiazolinyldene)-1,3-pentadienyl]-benzothiazolium iodide.

(b) *Specifications.* Dithiazanine iodide powder contains 200 milligrams of dithiazanine iodide per level standard tablespoon.

(c) *Sponsor.* See No. 054273 in § 510.600(c) of this chapter.

(d) *Conditions of use.* (1) Dithiazanine iodide powder is administered to dogs by mixing the proper dosage in the dog's food, using the following dosage schedule for various parasite infestations:

	Milligrams per pound of body weight	Length of treatment—days
Large roundworms (<i>Toxocara canis</i> , <i>Toxascaris leonina</i>).....	10	3-5
Hookworms (<i>Ancylostoma caninum</i> , <i>Uncinaria stenocephala</i>).....	10	7
Whipworms (<i>Trichuris vulpis</i>).....	10	7
Strongyloides (<i>Strongyloides canis</i> , <i>Strongyloides stercoralis</i>).....	10	10-12
Heartworm microfilariae (<i>Dirofilaria immitis</i>).....	3-5	7-10

Note: Treatment with dithiazanine iodide for heartworm microfilariae should follow 6 weeks after therapy for adult worms.

(2) The drug is contraindicated in animals sensitive to dithiazanine iodide and should be used cautiously, if at all, in dogs with reduced renal function.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(e) Use for treating dogs for large roundworms, hookworms, whipworms, and strongyloides as provided for in this section has been NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

[40 FR 13838, Mar. 27, 1975, as amended at 47 FR 51564, Nov. 16, 1982; 48 FR 32342, July 15, 1983; 53 FR 40727, Oct. 18, 1988]

§ 520.763c Dithiazanine iodide and piperazine citrate suspension.

(a) *Specifications.* Each milliliter of the drug contains 69 milligrams of

dithiazanine iodide and 83 milligrams of piperazine base (as piperazine citrate).

(b) *Sponsor.* See 054273 in § 510.600(c) of this chapter.

(c) *NAS/NRC status.* The conditions of use are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(d) *Conditions of use.*—(1) *Amount.* 1 ounce (30 milliliters) per 100 pounds of body weight for the first 500 pounds; ¼ ounce for each 100 pounds thereafter, up to 1,200 pounds; 10¼ ounces to animals over 1,200 pounds.

(2) *Indications for use.* For control of large roundworms, *Parascaris equorum*; small strongyles; large strongyles, *Strongylus vulgaris*; and pinworms, *Oxyuris equi*.

(3) *Limitations.* Administer by drench or mixed with the daily ration as a single dose. Treatment is recommended in spring and fall. In a heavily infested environment, treatment may be repeated every 30 days. Not for use in horses intended for food purposes. Severely debilitated animals should not be wormed except on the advice of a veterinarian. If the drug is for administration by stomach tube, it shall be labeled: "Federal law restricts this drug to use by or on the order of a licensed veterinarian."

[47 FR 52696, Nov. 23, 1982, as amended at 48 FR 32342, July 15, 1983; 53 FR 40727, Oct. 18, 1988]

§ 520.784 Doxylamine succinate tablets.

(a) *Specifications.* The drug is in tablet form and contains doxylamine succinate as the active drug ingredient.

(b) *Sponsor.* See No. 017220 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used in conditions in which antihistaminic therapy may be expected to alleviate some signs of disease in horses, dogs, and cats.¹

¹These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter.

(2) It is administered orally to horses at a dosage level of 1 to 2 milligrams per pound of body weight per day divided into 3 or 4 equal doses. It is administered orally to dogs and cats at a dosage level of 2 to 3 milligrams per pound of body weight per day divided into 3 or 4 equal doses.¹

(3) Not for use in horses intended for food.¹

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

[40 FR 13838, Mar. 27, 1975, as amended at 42 FR 60140, Nov. 25, 1977; 46 FR 48642, Oct. 2, 1981]

§ 520.812 Enrofloxacin tablets.

(a) *Specifications.* Each tablet contains either 5.7, 22.7, or 68.0 milligrams of enrofloxacin.

(b) *Sponsor.* See No. 000859 in § 510.600(c) of this chapter.

(c) *Conditions of use.*—(1) *Amount.* 2.5 mg/kg (1.13 mg/lb) of body weight twice daily.

(2) *Indications for use.* Dogs for treatment of the following bacterial infections: dermal infections (wounds and abscesses) caused by susceptible strains of *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, and *Staphylococcus aureus*; respiratory infections (pneumonia, tonsillitis, rhinitis) caused by susceptible strains of *Escherichia coli* and *Staphylococcus aureus*; and urinary cystitis caused by susceptible strains of *Escherichia coli*, *Proteus mirabilis*, and *Staphylococcus aureus*.

(3) *Limitations.* Treatment should be continued for 2 to 3 days beyond cessation of clinical symptoms. Do not use for more than 10 days. Safe use in breeding female dogs has not been established. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[54 FR 3444, Jan. 24, 1989]

§ 520.823 Erythromycin phosphate.

(a) *Specifications.* Erythromycin phosphate is the phosphate salt of the antibiotic substance produced by the growth of *Streptomyces erythreus* or the same antibiotic substance produced by any other means. One gram of erythromycin phosphate is equivalent

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lent to 0.89 gram of erythromycin master standard.

(b) *Sponsor.* See No. 050604 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See § 556.230 of this chapter.

(d) *Conditions of use.* It is used in drinking water as follows:

(1) *Broiler and replacement chickens*—(i) *Amount.* 0.500 gram per gallon.

(ii) *Indications for use.* As an aid in the control of chronic respiratory disease due to *Mycoplasma gallisepticum* susceptible to erythromycin.

(iii) *Limitations.* Administer for 5 days; do not use in replacement pullets over 16 weeks of age; do not use in chickens producing eggs for human consumption; to assure effectiveness, treated birds must consume enough medicated water to provide a therapeutic dosage; solutions older than 3 days should not be used; withdraw 1 day before slaughter.

(2) *Replacement chickens and chicken breeders*—(i) *Amount.* 0.500 gram per gallon.

(ii) *Indications for use.* As an aid in the control of infectious coryza due to *Hemophilus gallinarum* susceptible to erythromycin.

(iii) *Limitations.* Administer for 7 days; do not use in replacement pullets over 16 weeks of age; do not use in chickens producing eggs for human consumption; to assure effectiveness, treated birds must consume enough medicated water to provide a therapeutic dosage; solutions older than 3 days should not be used; withdraw 1 day before slaughter.

(3) *Growing turkeys*—(i) *Amount.* 0.500 gram per gallon.

(ii) *Indications for use.* As an aid in the control of blue comb (nonspecific infectious enteritis) caused by organisms susceptible to erythromycin.

(iii) *Limitations.* Administer for 7 days; do not use in turkeys producing eggs for human consumption; to assure effectiveness, treated birds must consume enough medicated water to provide a therapeutic dosage; solutions older than 3 days should not be used; withdraw 1 day before slaughter.

[40 FR 13838, Mar. 27, 1975, as amended at 45 FR 56798, Aug. 26, 1980]

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§ 520.863 Ethylisobutrazine hydrochloride tablets.

(a) *Specifications.* Each tablet contains either 10 milligrams or 50 milligrams of ethylisobutrazine hydrochloride.

(b) *Sponsor.* See No. 017220 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is administered orally to dogs as a tranquilizer.¹

(2) It is administered once daily at a dosage level of 2 to 5 milligrams of ethylisobutrazine hydrochloride per pound of body weight.¹

(3) It is not to be used in conjunction with organophosphates and/or procaine hydrochloride because phenothiazine may potentiate the toxicity of organophosphates and the activity of procaine hydrochloride.¹

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

[40 FR 13838, Mar. 27, 1975, as amended at 46 FR 48642, Oct. 2, 1981]

§ 520.903 Febantel oral dosage forms.

§ 520.903a Febantel paste.

(a) *Chemical name.* Dimethyl [(2-[(methoxyacetyl)amino]-4-(phenylthio)phenyl] carbonimidoyl]bis [carbamate].

(b) *Specifications.* The drug is a paste containing 45.5 percent febantel.

(c) *Sponsor.* See No. 000859 in § 510.600(c) of this chapter.

(d) *Conditions of use*—(1) *Amount.* Six milligrams per kilogram (2.73 milligrams per pound) of body weight in horses.

(2) *Indications for use.* For removal of large strongyles (*Strongylus vulgaris*, *S. edentatus*, *S. equinus*); ascarids (*Parascaris equorum*—sexually mature and immature); pinworms (*Oxyuris equi*—adult and 4th stage larva); and the various small strongyles in horses, foals, and ponies.

¹ These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(3) *Limitations.* (i) The paste may be administered on the base of the tongue or well mixed into a portion of the normal grain ration.

(ii) [Reserved]

(iii) For animals maintained on premises where reinfection is likely to occur, retreatment may be necessary. For most effective results, retreat in 6 to 8 weeks.

(iv) Not for use in horses intended for food.

(v) Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

43 FR 8797, Mar. 3, 1978; 43 FR 12311, Mar. 4, 1978, as amended at 43 FR 60882, Dec. 9, 1978. Redesignated at 45 FR 8587, Feb. 1980]

§ 520.903b Febantel suspension.

(a) *Specifications.* The suspension contains 9.3 percent (2.75 grams per ounce) febantel.

(b) *Sponsor.* See 000859 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* 3 milliliters per 100 pounds body weight (1 fluid ounce per 1000 pounds (6 milligrams per kilogram body weight)).

(2) *Indications for use.* For removal of ascarids (*Parascaris equorum*—adult and sexually immature), pinworms (*Oxyuris equi*—adult and 4th stage larvae), large strongyles (*Strongylus vulgaris*, *S. edentatus*, *S. edentatus*), and the various small strongyles in horses, breeding stallions and mares, pregnant mares, foals, and ponies.

(3) *Limitations.* Administer by stomach tube or drench, or by mixing well into a portion of the normal grain ration. For animals maintained on premises where reinfection is likely to occur, retreatment may be necessary. For most effective results, retreat in 6 to 8 weeks. Not for use in horses intended for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(d) *Special considerations.* Febantel suspension may be used in combination with trichlorfon oral liquid in accordance with the provisions of § 20.2520c, this section, and the following conditions:

(1) Combine 1 part febantel suspension with 5 parts trichlorfon liquid.

(2) Allow animal to consume a portion of daily grain ration; administer mixture by stomach tube at rate of 18 milliliters per 100 pounds of body weight.

[45 FR 8587, Feb. 8, 1980]

§ 520.903c Febantel-trichlorfon paste.

(a) *Specifications.* Each 40 grams of paste contains 2.7 grams of febantel and 16 grams of trichlorfon.

(b) *Sponsor.* See No. 000859 in § 510.600(c) of this chapter.

(c) *Special considerations.* The labeling shall bear the following statements: Trichlorfon is a cholinesterase inhibitor. Do not use simultaneously with, or within a few days before or after treatment with or exposure to, other cholinesterase-inhibiting drugs, pesticides, or chemicals. Do not administer in conjunction with, or within 1 week of use of, succinylcholine chloride, phenothiazine-derived tranquilizers, or anesthetics.

(d) *Conditions of use—(1) Amount.* 6 milligrams of febantel and 35 milligrams of trichlorfon per kilogram of body weight (40 grams of paste per 1,000-pound horse).

(2) *Indications for use.* For removal of large strongyles (*Strongylus vulgaris*, *S. edentatus*, *S. edentatus*), ascarids (*Parascaris equorum*—adult and sexually immature forms) pinworms (*Oxyuris equi*—adult and 4th stage larvae), small strongyles (various), and mouth and stomach stages of bots (*Gasterophilus intestinalis* and *G. nasalis*) in horses, stallions, breeding mares, pregnant mares, foals, and ponies.

(3) *Limitations.* For oral use in horses. Do not administer on an empty stomach. Not for use in horses intended for food. For horses maintained on premises where reinfection is likely to occur, retreatment may be required in 4 to 8 weeks. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

[48 FR 44204, Sept. 28, 1983]

§ 520.903d Febantel-praziquantel paste.

(a) *Specifications.* Each gram of paste contains 34 milligrams of febantel and 3.4 milligrams of praziquantel.

(b) *Sponsor.* See No. 000859 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount—(i) Dogs and cats* (over 6 months of age): 10 milligrams of febantel and 1 milligram of praziquantel per kilogram of body weight (1 gram of paste per 7.5 pounds body weight) administered by mouth or in the food once daily for 3 days.

(ii) *Puppies and kittens* (less than 6 months of age): 15 milligrams of febantel and 1.5 milligrams of praziquantel per kilogram of body weight (1 gram of paste per 5 pounds body weight) administered by mouth on a full stomach once daily for 3 days.

(2) *Indications for use.* (i) *Dogs and puppies:* For removal of hookworms (*Ancylostoma caninum* and *Uncinaria stenocephala*), whipworms (*Trichuris vulpis*), ascarids (*Toxocara canis* and *Toxascaris leonina*), and tapeworms (*Dipylidium caninum* and *Taenia pisiformis*).

(ii) *Cats and kittens:* For removal of hookworms (*Ancylostoma tubaeforme*), ascarids (*Toxocara cati*) and tapeworms (*Dipylidium caninum* and *Taenia taeniaeformis*).

(3) *Limitations.* Do not use in pregnant animals. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[50 FR 19167, May 7, 1985, as amended at 53 FR 48533, Dec. 1, 1988]

§ 520.905 Fenbendazole oral dosage forms.

§ 520.905a Fenbendazole suspension.

(a) *Chemical name.* Carbamic acid, [5-(phenylthio)-1*H*-benzimidazol-2-yl]-methyl ester.

(b) *Specifications.* The drug is a suspension containing 10 percent (100 milligrams per milliliter) fenbendazole.

(c) *Sponsor.* See No. 012799 in § 510.600(c) of this chapter.

(d) *Conditions of use—(1) Horses—(i) Amount.* 5 milligrams per kilogram (2.3 milligrams per pound) for the control of large strongyles, small strongyles, and pinworms; 10 milligrams per kilogram for the control of ascarids.

(ii) *Indications for use.* For the control of large strongyles (*Strongylus edentatus*, *S. equinus*, *S. vulgaris*), small strongyles (*Cyathostomum*

spp., *Cylicocyclus* spp., *Cylicostephanus* spp., *Triodontophorus* spp.), pinworms (*Oxyuris equi*), and ascarids (*Parascaris equorum*) in horses.

(iii) *Limitations.* Administer orally by dose syringe or suitable plastic syringe. Do not use in horses intended for food. Consult a veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

(2) *Cattle—(i) Amount.* Administer orally 5 milligrams per kilogram of body weight (2.3 milligrams per pound).

(A) *Indications for use.* For the removal and control of lungworm (*Dictyocaulus viviparus*); stomach worm (adults)—brown stomach worm (*Ostertagia ostertagi*); stomach worms (adults and 4th-stage larvae)—barber-pole worm (*Haemonchus contortus* and *H. placei*) and small stomach worm (*Trichostrongylus axei*); intestinal worms (adults and 4th-stage larvae)—hookworm (*Bunostomum phlebotomum*), threadnecked intestinal worm (*Nematodirus helvetianus*), small intestinal worm (*Cooperia punctata* and *C. oncophora*), bankrupt worm (*Trichostrongylus colubriformis*), and nodular worm (*Oesophagostomum radiatum*).

(B) *Limitations.* Retreatment may be needed after 4 to 6 weeks. Cattle must not be slaughtered within 8 days following last treatment. Do not use in dairy cattle of breeding age. Consult a veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

(ii) *Amount.* Administer orally 10 milligrams per kilogram of body weight.

(A) For the removal and control of stomach worm (4th-stage inhibited larvae/type II ostertagiasis), *Ostertagia ostertagi*, and tapeworm, *Moniezia benedeni*.

(B) *Limitations.* Retreatment may be needed after 4 to 6 weeks. Cattle must not be slaughtered within 8 days following last treatment. Do not use in dairy cattle of breeding age. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(e) *Special considerations.* Fenbendazole suspension 10 percent and approved forms of trichlorfon, when used concomitantly for treating the in-

dications provided in paragraph (d) of this section and for treating infections of stomach bot as provided in § 520.2520, have been shown to be compatible and not to interfere with one another.

[42 FR 59069, Nov. 15, 1977; 43 FR 12311, Mar. 24, 1978. Redesignated at 44 FR 1375, Jan. 5, 1979, and amended at 46 FR 29464, June 2, 1981; 47 FR 15327, Apr. 9, 1982; 48 FR 42809, Sept. 20, 1983; 49 FR 1983, Jan. 17, 1984; 53 FR 40056, Oct. 13, 1988]

§ 520.905b Fenbendazole granules.

(a) *Specifications.* The drug is in granular form containing 22 percent (222 milligrams per gram) fenbendazole.

(b) *Sponsor.* See No. 012799 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Horses—(i) Amount.* 5 milligrams per kilogram (2.3 milligrams per pound) for the control of large strongyles, small strongyles, and pinworms; 10 milligrams per kilogram for the control of ascarids.

(ii) *Indications for use.* For the control of infections of large strongyles (*Strongylus edentatus*, *S. equinus*, *S. vulgaris*), small strongyles, pinworms (*Oxyuris equi*), and ascarids (*Parascaris equorum*).

(iii) *Limitations.* Sprinkle the appropriate amount of drug on a small amount of the usual grain ration. Prepare for each horse individually. Withholding feed or water is not necessary. Retreat in 6 to 8 weeks if required. Do not use in horses intended for food. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

(2) *Dogs—(i) Amount.* 50 milligrams per kilogram (22.7 milligrams per pound) daily for 3 consecutive days.

(ii) *Indications for use.* For the removal of ascarids (*Toxocara canis*, *Toxascaris leonina*), hookworms (*Uncinostoma caninum*, *Uncinaria stenocephala*), whipworms (*Trichuris vulpis*), and tapeworms (*Taenia pistiformis*).

(iii) *Limitations.* Mix the appropriate amount of drug with a small amount of the usual food; dry dog food may require slight moistening to facilitate mixing. Medicated food must be fully consumed. Federal law re-

stricts this drug to use by or on the order of a licensed veterinarian.

[44 FR 1375, Jan. 5, 1979, as amended at 47 FR 15327, Apr. 9, 1982; 48 FR 50529, Nov. 2, 1983]

§ 520.905c Fenbendazole paste.

(a) *Specifications.* The product is an aqueous paste containing 10 percent fenbendazole.

(b) *Sponsor.* See No. 012799 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See § 556.275 of this chapter.

(d) *Conditions of use—(1) Horses—*

(i)(a) *Amount.* 2.3 milligrams per pound of body weight (one 2.5-gram fenbendazole syringe for a 1,100-pound horse). For foals and weanlings (less than 18 months of age), 4.6 milligrams per pound of body weight (one 2.5-gram fenbendazole syringe for each 550 pounds of body weight).

(b) *Indications for use.* For control of large strongyles (*Strongylus edentatus*, *S. equinus*, *S. vulgaris*), small strongyles, pinworms (*Oxyuris equi*), and ascarids (*Parascaris equorum*) in horses.

(c) *Limitations.* Retreatment at intervals of 6 to 8 weeks may be required. Do not use in horses intended for food. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

(ii)(a) *Amount.* 4.6 milligrams per pound of body weight (one 2.5-gram fenbendazole syringe for a 550-pound horse) daily for 5 days.

(b) *Indications for use.* For control of arteritis caused by the fourth stage larvae of *Strongylus vulgaris*.

(c) *Limitations.* Treatment should be initiated in the spring and repeated in 6 months. Do not use in horses intended for food. Consult your veterinarian for assistance in the diagnosis, treatment, and control of fourth stage larvae of *S. vulgaris*.

(2) *Cattle—(i) Amount.* Administer orally 5 milligrams per kilogram of body weight (2.3 milligrams per pound).

(ii) *Indications for use.* For the removal and control of lungworm (*Dictyocaulus viviparus*), barberpole worm (*Haemonchus contortus*), brown stomach worm (*Ostertagia ostertagi*), small

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stomach worm (*Trichostrongylus axei*), hookworm (*Bunostomum phlebotomum*), thread-necked intestinal worm (*Nematodirus helvetianus*), small intestinal worms (*Cooperia punctata* and *C. oncophora*), bankrupt worm (*Trichostrongylus colubriformis*), and nodular worm (*Oesophagostomum radiatum*).

(iii) *Limitations.* Re-treatment may be needed after 4 to 6 weeks. Cattle must not be slaughtered within 8 days following last treatment. Do not use in dairy cattle of breeding age. Consult a veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

(e) *Special considerations.* Fenbendazole paste 10 percent may be used concomitantly with approved forms of trichlorfon for the indications provided in paragraph (d)(1)(i) of this section and for treating infections of stomach bots as provided in § 520.2520.

[46 FR 32018, June 19, 1981, as amended at 47 FR 15327, Apr. 9, 1982; 49 FR 8433, Mar. 7, 1984; 50 FR 26358, June 26, 1985]

§ 520.905d Fenbendazole powder.

(a) *Specifications.* (1) Each 2-ounce packet contains 2.27 grams (4 percent) of fenbendazole plus other inert ingredients.

(2) Each 4-ounce packet contains 1.7 grams (1.5 percent) of fenbendazole plus other inert ingredients.

(b) *Sponsors.* (1) See No. 012799 in § 510.600(c) of this chapter for use of the 4-percent product.

(2) See No. 017800 in § 510.600(c) of this chapter for use of the 1.5-percent product.

(c) *Related tolerances.* See § 556.275 of this chapter.

(d) *Conditions of use.* It is administered to swine as follows:

(1) *Amount.* 3 milligrams fenbendazole per kilogram body weight per day (1.36 milligrams per pound per day).

(2) *Indications for use.* For removal and control of large roundworms (*Ascaris suum*); lungworms (*Metastrongylus apri*); nodular worms (*Oesophagostomum dentatum*, *O. quadrispinulatum*); small stomach worms (*Hyostrophylus rubidus*); whipworms (*Trichuris suis*); and kidneyworms (*Stephanurus dentatus*—mature and immature).

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(3) *Limitations.* Thoroughly mix the contents of the packet(s) with swine ration and administer according to label directions. Feed as sole ration for 3 consecutive days. Can be fed to pregnant sows. No prior withdrawal of feed or water is necessary. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

[49 FR 18090, Apr. 27, 1984, as amended at 49 FR 20485, May 15, 1984]

§ 520.905e Fenbendazole blocks.

(a) *Specifications.* Each pound of molasses block contains 750 milligrams of fenbendazole.

(b) *Sponsor.* See 012799 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See § 556.275 of this chapter.

(d) *Conditions of use.*—(1) *Amount.* 0.1 pound of block per 100 pounds of body weight per day for 3 days. Total dose for the 3-day period is 2.27 milligrams of fenbendazole per pound of body weight for mature cattle.

(2) *Indications for use.* For removal and control of infections of lungworms (*Dictyocaulus viviparus*) and gastrointestinal roundworms (*Haemonchus contortus*, *Ostertagia ostertagi*, *Trichostrongylus axei*, *Bunostomum phlebotomum*, *Nematodirus helvetianus*, *Cooperia oncophora* and *C. punctata*, *Trichostrongylus colubriformis*, and *Oesophagostomum radiatum*) in beef cattle.

(3) *Limitations.* Administer free choice to beef cattle on pasture that have become accustomed to nonmedicated block feeding during an adaptation period of 12 to 19 days. Cattle must not be slaughtered within 11 days following last treatment. Animals maintained under conditions of constant worm exposure may require re-treatment within 6 to 8 weeks. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

[51 FR 41783, Nov. 19, 1986]

§ 520.960 Flumethasone tablets.

(a) *Specifications.* Each tablet contains 0.0625 milligram of flumethasone.

(b) *Sponsor.* See No. 000033 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* (i) Dogs: Administer orally from 0.0625 to 0.25 milligram daily in divided doses.

(ii) Cats: Administer orally from 0.03125 to 0.125 milligram daily in divided doses.

(2) *Indications for use.* (i) Dogs: It is used for musculoskeletal conditions due to inflammation of muscles or joints and accessory structures, where permanent structural changes do not exist, such as arthritis, the disc syndrome, and myositis.

(ii) Dogs and cats: It is used in certain acute and chronic dermatoses of varying etiology to help control the pruritus, irritation, and inflammation associated with these conditions.

(3) *Limitations.* Do not use in viral infections. Anti-inflammatory action of corticosteroids may mask signs of infection. Do not use in animals with tuberculosis, chronic nephritis, cushingoid syndrome, or where peptic ulcers occur, except for emergency therapy. Clinical and experimental data have demonstrated that corticosteroids administered orally or parenterally to animals may induce the first stage of parturition when administered during last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[44 FR 7131, Feb. 6, 1979]

§ 520.970 Flunixin oral dosage forms.

§ 520.970a Flunixin meglumine granules.

(a) *Specifications.* Each 10-gram packet contains flunixin meglumine equivalent to 250 milligrams of flunixin.

(b) *Sponsor.* No. 000061 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* 0.5 milligram of flunixin per pound of body weight (one packet per 500 pounds) per day.

(2) *Indications for use.* For alleviation of inflammation and pain associated with musculoskeletal disorders in the horse.

(3) *Limitations.* Administer daily dose for up to 5 days by sprinkling on small amount of feed. The effect of this drug on pregnancy has not been determined. Not for use in horses intended for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[44 FR 36381, June 22, 1979. Redesignated at 50 FR 38114, Sept. 20, 1985, and amended at 52 FR 7832, Mar. 13, 1987]

§ 520.970b Flunixin meglumine paste.

(a) *Specifications.* Each 30-gram syringe contains flunixin meglumine equivalent to 1,500 milligrams of flunixin.

(b) *Sponsor.* No. 000061 in § 510.600(c) of this chapter.

(c) *Conditions of use. Horses—(1) Amount.* 0.5 milligram of flunixin per pound of body weight daily.

(2) *Indications for use.* For alleviation of inflammation and pain associated with musculoskeletal disorders.

(3) *Limitations.* For oral use only. Treatment should not exceed 5 consecutive days. The effect of this drug on pregnancy has not been determined. Not for use in horses intended for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[50 FR 38114, Sept. 20, 1985, as amended at 52 FR 7832, Mar. 13, 1987]

§ 520.1010 Furosemide oral dosage forms.

§ 520.1010a Furosemide tablets or boluses.

(a) *Specifications.* Each tablet contains 12.5 or 50 milligrams of furosemide. Each bolus contains 2 grams of furosemide.

(b) *Sponsor.* See No. 012799 in § 510.600(c) of this chapter for conditions of use provided for in paragraphs (c) (1) and (2) of this section; see Nos. 000725 and 054273 in § 510.600(c) of this chapter for use in dogs as provided for in paragraph (c)(1) of this section; see No. 000332 in § 510.600(c) of this chapter for use of a 12.5- and 50-milligram tablet for conditions of use provided for in paragraph (c)(3) of this section.

(c) *Conditions of use.* It is used as follows:

(1) *Dogs and cats*—(i) *Amount*. 1 to 2 milligrams per pound of body weight, once or twice daily, with a 6- to 8-hour interval between successive daily doses.

(ii) *Indications for use*. It is used for the treatment of edema (pulmonary congestion, ascites) associated with cardiac insufficiency and acute noninflammatory tissue edema.

(iii) *Limitations*. The dosage should be adjusted to the animal's response. In severe edematous or refractory cases, the dosage may be doubled or increased by increments of 1 milligram per pound of body weight to establish the effective dose. This dose should be administered once or twice daily on an intermittent schedule. Diuretic therapy should be discontinued after reduction of edema, or when necessary, maintained after determining a programmed dosage schedule to prevent recurrence. The drug, if given in excessive amounts or over extended periods of time may result in dehydration and/or electrolyte imbalance. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(2) *Cattle*—(i) *Amount*. 1 to 2 milligrams per pound of body weight, or one 2-gram bolus per animal, per day.

(ii) *Indications for use*. The drug is used for the treatment of physiological parturient edema of the mammary gland and associated structures.

(iii) *Limitations*. Treatment not to exceed 48 hours post-parturition. For oral use only. When treatment is initiated with an injectable, it is followed by a 12-hour interval, and maintained by oral administration. Milk taken during treatment and for 48 hours (four milkings) after the last treatment must not be used for food. Cattle must not be slaughtered for food within 48 hours following last treatment. The drug, if given in excessive amounts or over extended periods of time, may result in dehydration and/or electrolyte imbalance. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(3) *Dogs*—(i) *Amount*. 1 to 2 milligrams per pound of body weight, once or twice daily, with a 6- to 8-hour interval between successive daily doses.

(ii) *Indications for use*. It is used for the treatment of edema (pulmonary

congestion, ascites) associated with cardiac insufficiency.

(iii) *Limitations*. The dosage should be adjusted to the animal's response. In severe cases, the dosage may be doubled or increased by increments of 1 milligram per pound of body weight to establish the effective dose. This dose should be administered once or twice daily on an intermittent schedule. Diuretic therapy should be discontinued after reduction of edema, or when necessary, maintained after determining a programmed dosage schedule to prevent recurrence. The drug, if given in excessive amounts or over extended periods of time, may result in dehydration and/or electrolyte imbalance. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[41 FR 52446, Nov. 30, 1976. Redesignated at 43 FR 14647, Apr. 7, 1978, and amended at 48 FR 40517, Sept. 8, 1983; 48 FR 49841, Oct. 28, 1983; 53 FR 40727, Oct. 18, 1988]

§ 520.1010b Furosemide powder.

(a) *Specifications*. Furosemide powder is packaged in packets containing 2 grams of furosemide plus other inert ingredients.

(b) *Sponsor*. See No. 012799 in § 510.600(c) of this chapter.

(c) *Conditions of use*. It is administered to dairy cattle alone, as a "top dressing" upon a small amount of feed or as a drench.

(1) *Amount*. 1 to 2 milligrams per pound of body weight but not to exceed one packet per animal, per day.

(2) *Indications for use*. The drug is used for the treatment of physiological parturient edema of the mammary gland and associated structures.

(3) *Limitations*. Treatment not to exceed 48 hours post-parturition. For oral use only. The individual dose is one packet administered once daily; when treatment is initiated with an injectable, at least a 12-hour interval must follow before oral administration. Milk taken during treatment and for 48 hours (four milkings) after the last treatment must not be used for food. Cattle must not be slaughtered for food within 48 hours following last treatment. The drug, if given in excessive amounts or over extended periods

of time, may result in dehydration and electrolyte imbalance. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[43 FR 14847, Apr. 7, 1978, as amended at 47 FR 15327, Apr. 9, 1982]

§ 520.1010c Furosemide syrup.

(a) *Specifications.* Each milliliter of syrup contains 10 milligrams of furosemide.

(b) *Sponsor.* See No. 012799 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* 1 to 2 milliliters orally (10 to 20 milligrams) per 10 pounds of body weight (approximately 2.5 to 5 milligrams per kilogram), once or twice daily, with a 6- to 8-hour interval between successive daily doses.

(2) *Indications for use.* It is used in dogs for the treatment of edema (pulmonary congestion, ascites) associated with cardiac insufficiency and acute noninflammatory tissue edema.

(3) *Limitations.* The dosage should be adjusted to the animal's response. In severe edematous or refractory cases, the dosage may be doubled or increased by increments of 1 milligram per pound of body weight to establish the effective dose. This dose should be administered once or twice daily on an intermittent schedule. Diuretic therapy should be discontinued after reduction of edema or, when necessary, maintained after determining a programmed dosage schedule to prevent recurrence. If given in excessive amounts or over extended periods of time, the drug may result in dehydration and/or electrolyte imbalance. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[43 FR 11177, Mar. 17, 1978, as amended at 47 FR 15327, Apr. 9, 1982]

§ 520.1044 Gentamicin sulfate oral dosage forms.

[49 FR 572, Jan. 5, 1984]

§ 520.1044a Gentamicin sulfate oral solution.

(a) *Specifications.* Each milliliter of aqueous solution contains gentamicin sulfate equivalent to 50 milligrams of gentamicin.

(b) *Sponsor.* See No. 000061 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See § 556.300 of this chapter.

(d) *Conditions of use—(1) Amount.* Colibacillosis: 1 milliliter per 2 gallons of drinking water for 3 consecutive days, to provide 0.5 milligram/pound/day; swine dysentery: 1 milliliter per 1 gallon of drinking water for 3 consecutive days, to provide 1.0 milligram/pound/day.

(2) *Indications for use.* In weanling swine for control and treatment of colibacillosis caused by strains of *E. coli* sensitive to gentamicin, and in swine for control and treatment of swine dysentery associated with *Treponema hyodysenteriae*.

(3) *Limitations.* For use in swine drinking water only. Do not store or offer medicated drinking water in rusty containers since the drug is quickly destroyed in such containers. Medicated drinking water should be prepared daily and be the sole source of drinking water for 3 consecutive days. Treatment may be repeated if dysentery recurs. Do not slaughter treated swine for food for at least 3 days following treatment.

[48 FR 10302, Mar. 11, 1983. Redesignated at 49 FR 572, Jan. 5, 1984, and amended at 49 FR 14332, Apr. 11, 1984; 52 FR 7832, Mar. 13, 1987]

§ 520.1044b Gentamicin sulfate pig pump oral solution.

(a) *Specifications.* Each milliliter of pig pump oral solution contains gentamicin sulfate equivalent to 4.35 milligrams of gentamicin.

(b) *Sponsor.* See No. 000061 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See § 556.300 of this chapter.

(d) *Conditions of use—(1) Amount.* Administer 1.15 milliliters of pig pump oral solution (5 milligrams of gentamicin) orally per pig one time.

(2) *Indications for use.* In neonatal swine 1 to 3 days of age for control and treatment of colibacillosis caused by strains of *E. coli* sensitive to gentamicin.

(3) *Limitations.* For use in neonatal swine only. Do not slaughter treated

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swine for food for at least 14 days following treatment.

[49 FR 572, Jan. 5, 1984, as amended at 52 FR 7832, Mar. 13, 1987]

§ 520.1044c Gentamicin sulfate soluble powder.

(a) *Specifications.* Each gram of gentamicin sulfate soluble powder contains gentamicin sulfate equivalent to 16.7, 66.7, or 333.3 milligrams of gentamicin.

(b) *Sponsor.* See No. 000061 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See § 556.300 of this chapter.

(d) *Conditions of use—(1) Amount.* Colibacillosis: gentamicin sulfate equivalent to 25 milligrams of gentamicin per gallon of drinking water for 3 consecutive days, to provide 0.5 milligram per pound of body weight per day; swine dysentery: gentamicin sulfate equivalent to 50 milligrams of gentamicin per gallon of drinking water for 3 consecutive days, to provide 1 milligram per pound of body weight per day.

(2) *Indications for use.* In weanling swine for control and treatment of colibacillosis caused by strains of *E. coli* sensitive to gentamicin, and in swine for control and treatment of swine dysentery associated with *Treponema hyodysenteriae*.

(3) *Limitations.* For use in swine drinking water only. Do not store or offer medicated drinking water in rusty containers since the drug is quickly destroyed in such containers. Medicated drinking water should be prepared daily and be the sole source of drinking water for 3 consecutive days. Treatment may be repeated if dysentery recurs. Do not slaughter treated swine for food for at least 10 days following treatment.

[49 FR 29778, July 24, 1984, as amended at 52 FR 7832, Mar. 13, 1987; 52 FR 48675, Dec. 24, 1987]

§ 520.1065 Glycobiarsol tablets.

(a) *Specifications.* Each tablet contains 1 or 2.5 grams of glycobiarsol.

(b) *Sponsor.* See No. 000934 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* 100 milligrams per pound of body

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weight (one 1-gram tablet per 10 pounds or one 2.5-gram tablet per 25 pounds of body weight) once daily for 5 consecutive days.

(2) *Indications for use.* For elimination of whipworms (*Trichuris vulpis*) from dogs.

(3) *Limitations.* Administer tablets orally or crush and mix in feed. If required, animals can be retreated 2 to 4 weeks after first treatment. Fasting is not required prior to treatment, and no purgation is needed following treatment. Administer with caution to severely debilitated and emaciated animals. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[43 FR 30274, Aug. 14, 1978]

§ 520.1100 Griseofulvin.

(a) *Chemical name.* 7-Chloro-2',4,6-trimethoxy-6'-methylspiro [benzofuran-2(3H), 1'-(2)-cyclohexene]-3,4'-dione.

(b) *Specifications.* Complies with U.S.P. for griseofulvin microsize.

(c) *Sponsor.* (1) See No. 000061 in § 510.600(c) of this chapter for the sponsor of the usages provided by paragraphs (d)(1), (3), and (4) of this section.

(2) [Reserved]

(3) See No. 011716 in § 510.600(c) of this chapter for the sponsor of the usages provided by paragraph (d)(4) of this section.

(d) *Conditions of use.* (1) As a soluble powder for horses, it is administered as a drench or as a top dressing on feed. It is used for equine ringworm infection caused by *Trichophyton equinum* or *Microsporum gypseum*. Administer for not less than 10 days a daily dose as follows: Adults, 2.5 grams; yearlings, 1.25 to 2.5 grams; and foals, 1.25 grams. Not for use in horses intended for food. For use only by or on the order of a licensed veterinarian.

(2) [Reserved]

(3)(i) Boluses containing 2.5 grams of griseofulvin are used in horses for treating ringworm infection caused by *Trichophyton equinum*. It is administered to adult horses at a level of one bolus per day, to yearlings at one-half to one bolus per day, and to foals at one-half bolus per day. All three

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dosage levels should be administered for a period of not less than 10 days. In responsive cases, treatment should be continued until all infected areas are proven negative by appropriate culture. Not for use in horses intended for food.

(ii) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(4) Dogs and cats: (i) *Amount*. 125- and 500-milligram tablets administered orally as follows:

(a) Daily (single or divided) dose:

Body weight (pounds)	Dosage (milligrams)
Up to 6	62.5
6 to 18	125
18 to 36	250
36 to 48	375
48 to 75	500

(b) Weekly (single) dose: If experience indicates that treatment is more effective for the drug given in large doses, administer at intervals of 7 to 10 days, a dose equal to 10 milligrams/pound of body weight x body weight x number of days between treatments. Dosage should be adjusted according to response. Administer additional dose after the animal is free of infection.

(ii) *Indications for use*. For treatment of fungal infections of the skin, hair, and claws caused by *Trichophyton mentagrophytes*, *T. rubrum*, *T. schoenleini*, *T. sulphurem*, *T. verrucosum*, *T. interdigitale*, *Epidermophyton floccosum*, *Microsporum gypseum*, *M. canis*, *M. audouini*.

(iii) *Limitations*. For satisfactory diagnosis, a microscopic tissue examination or culture is recommended prior to treatment. Treatment should be continued for 3 to 4 weeks in skin and hair infections, and up to 4 months for infections involving nails or claws. Clipping of hair, nails, and claws to help remove any remaining viable fungi is indicated. Safety for use of griseofulvin for pregnant animals has not been established. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13838, Mar. 27, 1975, as amended at 41 FR 42948, Sept. 29, 1976; 43 FR 28458, June 30, 1978; 52 FR 7832, Mar. 13, 1987]

§ 520.1120 Haloxon oral dosage forms.

§ 520.1120a Haloxon drench.

(a) *Chemical name*. 3-Chloro-7-hydroxy-4-methylcoumarin bis (2-chloroethyl) phosphate.

(b) *Specifications*. Haloxon assay of not less than 96 percent by infrared spectrum at 8.62 microns.

(c) *Sponsor*. See No. 017220 in § 510.600(c) of this chapter.

(d) *Special considerations*. Do not use any drug, insecticide, pesticide, or other chemical having cholinesterase-inhibiting activity either simultaneously or within a few days before or after treatment with haloxon.

(e) *Related tolerances*. See § 556.310 of this chapter.

(f) *Conditions of use*. It is used as a drench as follows:

(1) *Cattle* —(i) *Amount*. 141.5 grams per packet.

(ii) *Indications for use*. Control of gastrointestinal roundworms of the genera *Haemonchus*, *Ostertagia*, *Trichostrongylus*, and *Cooperia*.

(iii) *Limitations*. (a) Dissolve each packet in 32 fluid ounces of water and administer as follows:

Weight of animal (pounds)	Dose (fluid ounces)
Up to 100	1/2
100 to 150	3/4
150 to 200	1
200 to 300	1 1/2
300 to 450	2
450 to 700	3
700 to 1,000	4
1,000 to 1,200	5
Over 1,200	6

(b) Do not treat within 1 week of slaughter; do not treat dairy animals of breeding age; animals should be re-treated in 3 to 4 weeks.

[40 FR 13838, Mar. 27, 1975, as amended at 45 FR 10333, Feb. 15, 1980; 46 FR 48642, Oct. 2, 1981]

§ 520.1120b Haloxon boluses.

(a) *Chemical name*. 3-Chloro-7-hydroxy-4-methylcoumarin bis (2-chloroethyl) phosphate.

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(b) *Specifications.* Each bolus contains 10.1 grams of haloxon.

(c) *Sponsor.* See No. 017220 in § 510.600(c) of this chapter.

(d) *Related tolerances.* See § 556.310 of this chapter.

(e) *Conditions of use.* (1) Haloxon bolus is an anthelmintic used in cattle for the control of gastrointestinal roundworms of the genera *Haemonchus*, *Ostertagia*, *Trichostrongylus* and *Cooperia*.

(2) It is administered by giving one bolus per approximately 500 pounds body weight (35 to 50 milligrams per kilogram of body weight).

(3) For most effective results, retreat animals in 3 to 4 weeks. If reinfection is likely to occur, additional retreatments may be necessary.

(4) Do not use any drug, pesticide or other chemical having cholinesterase inhibiting activity either simultaneously or within a few days before or after treatment with haloxon.

(5) Do not treat animals within one week of slaughter.

(6) Do not treat dairy animals of breeding age or older.

[40 FR 13838, Mar. 27, 1975, as amended at 44 FR 61591, Oct. 29, 1979; 46 FR 48642, Oct. 2, 1981]

§ 520.1157 Iodinated casein tablets.

(a) *Specifications.* Each 1-gram tablet contains 25 milligrams of iodinated casein.

(b) *Sponsor.* See No. 017762 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* $\frac{1}{2}$ to 1 tablet per 10 pounds of body weight (equivalent to 0.5 to 2.5 milligrams of iodinated casein per pound of body weight).

(2) *Indications for use.* For dogs for apparent decreased thyroid activity where the signs are alopecia, scaliness of the skin surface, loss of hair, seborrhea, thickening of the skin, hyperpigmentation, and lethargy.

(3) *Limitations.* If no response is observed in 30 to 45 days, the drug should be withdrawn and the diagnosis reconsidered. Do not use in the presence of cardiac disease, ischemia, adrenal insufficiency, or nephrosis. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

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[49 FR 22469, May 30, 1984]

§ 520.1158 Iodochlorhydroxyquin boluses.

(a) *Specifications.* Each bolus contains 10 grams of iodochlorhydroxyquin.

(b) *Sponsor.* See No. 053501 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* 1 bolus (10 grams) daily for a 1,000-pound horse.

(2) *Indications for use.* For treatment of equine diarrhea.

(3) *Limitations.* For horses only; not to be administered to food-producing animals. Do not administer to horses intended for use as food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[48 FR 8054, Feb. 25, 1983, as amended at 50 FR 41489, Oct. 11, 1985]

§ 520.1182 Iron dextran oral suspension.

(a) *Specifications.* Each 1.8 milliliter contains 100 milligrams of elemental iron as ferric hydroxide in complex with a low molecular weight dextran and 0.2 percent phenol as a preservative.

(b) *Sponsor.* See 017800 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* 100 milligrams of elemental iron to each pig.

(2) *Indications for use.* Prevention of iron deficiency anemia in baby pigs.

(3) *Limitations.* Treat each pig within 24 hours of farrowing. Administer 1.8 milliliters orally by automatic dose dispenser.

[45 FR 75199, Nov. 14, 1980]

§ 520.1192 Ivermectin paste.

(a) *Specifications—(1) Horses.* Paste contains 1.87 percent ivermectin.

(2) *Cattle.* Paste contains 0.153 percent ivermectin.

(b) *Sponsor.* See No. 000006 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Horses—(i) Amount.* 200 micrograms per kilogram (91 micrograms per pound) of body weight.

(ii) *Indications for use.* It is used in horses for the treatment and control of large strongyles (adult) (*Strongylus equinus*), (adult and arterial larval stages) (*Strongylus vulgaris*), (adult

and migrating tissue stages) (*Strongylus edentatus*), (adult) (*Triodontophorus* spp.); small strongyles, including those resistant to some benzimidazole class compounds (adult and fourth stage larvae) (*Cyathostomum* spp., *Cylicocycylus* spp., *Cylicodontophorus* spp., *Cylicostephanus* spp.); pinworms (adult and fourth stage larvae) (*Oxyuris equi*); ascarids (third- and fourth-stage larvae and adults) (*Parascaris equorum*); hairworms (adult) (*Trichostrongylus axei*); large mouth stomach worms (adult) (*Habronema muscae*); stomach bots (oral and gastric stages) (*Gastrophilus* spp.); lungworms (adults and fourth stage larvae) (*Dictyocaulus arnfieldi*); intestinal threadworms (adults) (*Strongyloides westeri*); summer sores caused by *Habronema* and *Draschia* spp. cutaneous third stage larvae; and dermatitis caused by neck threadworm microfilariæ (*Onchocerca* spp.).

(iii) *Limitations*. For oral use only. Do not use in horses intended for food purposes. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

(2) *Cattle*—(i) *Amount*. 23 milligrams per 250 pounds of body weight.

(ii) *Indications for use*. It is used in cattle for the treatment and control of gastrointestinal roundworms (adults and fourth-stage larvae) (*Ostertagia ostertagi* (including inhibited forms), *O. lyrata*, *Haemonchus placei*, *Trichostrongylus axei*, *T. colubriiformis*, *Cooperia oncophora*, *C. punctata*, *Nematodirus helvetianus*, *Bunostomum phlebotomum*, *Strongyloides papillosus* (adults only), *Oesophagostomum radiatum*, *Trichuris ovis* (adults only)); lungworms (adults and fourth-stage larvae) (*Dictyocaulus viviparus*); grubs (first, second, and third instars) (*Hypoderma bovis*, *H. lineatum*); and sucking lice (*Linognathus vituli*, *Haematopinus eurysternus*).

(iii) *Limitations*. For oral use only. Do not treat cattle within 24 days of slaughter. Because withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

[49 FR 22275, May 29, 1984, as amended at 50 FR 27819, July 8, 1985; 51 FR 44449, Dec. 10, 1986; 53 FR 51273, Dec. 21, 1988]

§ 520.1193 Ivermectin tablets.

(a) *Specifications*. Each tablet contains 68, 136, or 272 micrograms of ivermectin.

(b) *Sponsor*. See 000006 in § 510.600(c) of this chapter.

(c) *Conditions of use in dogs*—(1) *Amount*. 6.0 micrograms per kilogram body weight (2.72 micrograms per pound), minimum. For dogs up to 25 pounds, 68 micrograms; dogs 26 to 50 pounds, 136 micrograms; dogs 51 to 100 pounds, 272 micrograms; dogs over 100 pounds, a combination of the appropriate tablets. The drug is administered at monthly dosing intervals.

(2) *Indications for use*. To prevent canine heartworm disease (*Dirofilaria immitis* infection) by eliminating the tissue stage of larvae.

(3) *Limitations*. Use once-a-month. Not for use in dogs under 6 weeks old. Initial use within a month after first exposure to mosquitoes. Final use within a month after last exposure to mosquitoes. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[52 FR 11042, Apr. 7, 1987]

§ 520.1194 Ivermectin drench.

(a) *Specifications*. Each milliliter of 0.08 percent (weight per volume) micellar solution contains 0.08 milligram of ivermectin.

(b) *Sponsor*. See No. 000006 in § 510.600(c) of this chapter.

(c) *Related tolerances*. See § 556.344 of this chapter.

(d) *Conditions of use*—(1) *Amount*. 3.0 milliliters (2.4 milligrams of ivermectin) per 26 pounds of body weight (or 200 micrograms per kilogram of body weight).

(2) *Indications for use*. It is used in sheep for treatment and control of the adult and fourth-stage larvae of the following parasites of sheep: gastrointestinal roundworms (*Haemonchus contortus*, *H. placei* (adults only), *Ostertagia circumcincta*, *Trichostrongylus axei*, *T. Colubriiformis*, *Cooperia oncophora* (adults only), *C. curticei*, *Oesophagostomum columbianum*, *O.*

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venulosum (adults only), *Nematodirus battus*, *N. spathiger*, *Strongyloides papillosus* (adults only), *Chabertia ovina* (adults only), *Trichuris ovis* (adults only), lungworms (*Dictyocaulus filaria*); and all larval stages of the nasal bot *Oestrus ovis*.

(3) *Limitations.* It is used as a drench in sheep only. Do not treat sheep within 11 days of slaughter. Do not use in other animal species as severe adverse reactions, including fatalities in dogs, may result. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

[53 FR 27958, July 26, 1988]

§ 520.1195 Ivermectin liquid.

(a) *Specifications.* Each milliliter contains 10 milligrams of ivermectin.

(b) *Sponsor.* See No. 000006 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* 200 micrograms per kilogram of body weight as a single dose.

(2) *Indications for use.* It is used in horses for the treatment and control of large strongyles (adult) (*Strongylus equinus*), (adult and arterial larval stages) (*Strongylus vulgaris*), (adult and migrating tissue stages) (*Strongylus edentatus*), (adult) (*Triodontophorus* spp.); small strongyles, including those resistant to some benzimidazole class compounds (adult and fourth stage larvae) (*Cyathostomum* spp., *Cylicocyclus* spp., *Cylicodontophorus* spp., *Cylicostephanus* spp.); pinworms (adult and fourth stage larvae) (*Oxyuris equi*); ascarids (third- and fourth-stage larvae and adults) (*Parascaris equorum*); hairworms (adult) (*Trichostrongylus axei*); large mouth stomach worms (adult) (*Habronema muscae*); stomach bots (oral and gastric stages) (*Gastrophilus* spp.); lungworms (adults and fourth stage larvae) (*Dictyocaulus arnfieldi*); intestinal threadworms (adults) (*Strongyloides westeri*); summer sores caused by *Habronema* and *Draschia* spp. cutaneous third stage larvae; and dermatitis caused by neck threadworm microfilariae (*Onchocerca* spp.).

(3) *Limitations.* Administer by stomach tube or as an oral drench. Do not use in horses intended for food purposes. Federal law restricts this drug

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to us by or on the order of a licensed veterinarian.

[52 FR 34637, Sept. 14, 1987, as amended at 53 FR 51273, Dec. 21, 1988]

§ 520.1204 Kanamycin sulfate, aminopen-
tamide hydrogen sulfate, pectin, bis-
muth subcarbonate, activated attapul-
gite oral.

(a) *Specifications.* Each tablet or each five milliliters of suspension of the drug contains: 100 milligrams of kanamycin as the sulfate (the kanamycin used conforms to the standards of identity, strength, quality, and purity prescribed by § 444.30 of this chapter), 0.033 milligram of aminopen-
tamide hydrogen sulfate, 25 milligrams of pectin, 250 milligrams of bismuth subcarbonate, and 500 milligrams of activated attapul-
gite.

(b) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is administered orally to dogs for the symptomatic relief of acute bacterial diarrhea caused by kanamycin-susceptible organisms.

(2) The drug is recommended for use at the rate of one tablet or one teaspoonful (5 milliliters) of suspension per 20 pounds of body weight every 8 hours. Animals weighing under 10 pounds should be given one-half the above amount every 8 hours. The initial dose should be twice the amount of a single dose. Maximum dosage should not exceed three times the recommended dose.

(3) For use only by or on the order of a licensed veterinarian.

[40 FR 13838, Mar. 27, 1975, as amended at 53 FR 27851, July 25, 1988]

§ 520.1236 Lenperone tablets.

(a) *Specifications.* Each tablet contains 5, 10, or 25 milligrams of lenperone hydrochloride.

(b) *Sponsor.* See No. 000031 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) Used in dogs as a tranquilizer, antiemetic, and for pre- and postoperative medication.

(2) Administered orally at .25 to 1.0 milligram per pound of body weight, every 5 to 8 hours.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[46 FR 25085, May 5, 1981, as amended at 51 FR 42834, Nov. 26, 1986]

§ 520.1242 Levamisole hydrochloride oral dosage forms.

§ 520.1242a Levamisole hydrochloride drench and drinking water.

(a) *Chemical name.* (-)-2,3,5,6-Tetrahydro-6-phenylimidazo [2,1-b] thiazole monohydrochloride.

(b) *Specifications.* Assay of not less than 98 percent by nonaqueous titration with 0.1N potassium isopropoxide; 1 isomer minimum 95 percent pure by optical rotation.

(c) *Sponsor.* (1) See No. 043781 in § 510.600(c) of this chapter for conditions of use provided for in paragraph (f) of this section.

(2) See 011716 in § 510.600(c) of this chapter for conditions of use provided for in paragraphs (f) (1) and (2)(ii), and (f)(3) (for 18.15 grams per bottle), of this section.

(d) [Reserved]

(e) *Related tolerances.* Section 556.350 of this chapter.

(f) *Conditions of use.* It is used as follows:

(1) *Cattle*—(i) *Amount.* 46.8 grams per packet.

(ii) *Indications for use.* Anthelmintic effective against the following nematode infections: Stomach worms (*Haemonchus*, *Trichostrongylus*, *Ostertagia*), intestinal worms (*Trichostrongylus*, *Cooperia*, *Nematodirus*, *Bunostomum*, *Oesophagostomum*), and lungworms (*Dictyocaulus*).

(iii) *Limitations.* Dissolve in water to provide 32 fluid ounces of drench solution and administer as a drench at ¼ ounce 0.365 gram) per 100 pounds of body weight as a single dose; or dissolve in water to provide 8.75 fluid ounces of concentrate solution and administer as a drench at 2 cubic centimeters (0.365 gram) per 100 pounds of body weight as a single oral dose by syringe; conditions of constant helminth exposure may require retreatment within 2 to 4 weeks after the first treatment; do not slaughter for food within 48 hours of treatment; not for use in dairy animals of breeding

age; consult veterinarian before using in severely debilitated animals.

(2) *Sheep*—(i) *Amount.* 46.8 grams per packet.

(a) *Indications for use.* Anthelmintic effective against the following nematode infections: Stomach worms (*Haemonchus*, *Trichostrongylus*, *Ostertagia*), intestinal worms (*Trichostrongylus*, *Cooperia*, *Nematodirus*, *Bunostomum*, *Oesophagostomum*, *Chabertia*), and lungworms (*Dictyocaulus*).

(b) *Limitations.* Dissolve in 1 gallon (128 fluid ounces) of water and administer as a single drench at 1 ounce (0.365 gram) per 100 pounds of body weight; conditions of constant helminth exposure may require retreatment within 2 to 4 weeks after the first treatment; do not slaughter for food within 72 hours of treatment; consult veterinarian before using in severely debilitated animals.

(ii) *Amount.* 11.7 grams per packet.

(a) *Indications for use.* See paragraph (f)(2)(1)(a) of this section.

(b) *Limitations.* Dissolve in 1 quart (32 fluid ounces) of water and administer as a single drench at 1 ounce (0.365 gram) per 100 pounds of body weight or dissolve 1 packet in 10.9 fluid ounces of water and administer as a single drench at 1 cubic centimeter (0.036 gram) per 10 pounds of body weight; conditions of constant helminth exposure may require retreatment within 2 to 4 weeks after the first treatment; do not slaughter for food within 72 hours of treatment; consult veterinarian before using in severely debilitated animals.

(3) *Swine*—(i) *Amount.* 9.075 or 18.15 grams per bottle.

(ii) *Indications for use.* Anthelmintic effective against the following nematode infections: Large roundworms (*Ascaris suum*), nodular worms (*Oesophagostomum* spp.), intestinal thread worms (*Strongyloides ransomi*) and lungworms (*Metastrongylus* spp.).

(iii) *Limitations.* Dissolve in water to provide 9.075 grams per 250 milliliters or 18.15 grams per 500 milliliters. Add 10 milliliters (2 teaspoons) of this concentrate solution to each gallon of drinking water. Allow 1 gallon of medicated drinking water for each 100 pounds of body weight of pigs to be treated. No other source of water

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should be offered. After pigs have consumed medicated water, resume use of regular water. Pigs maintained under conditions of constant exposure to worms may require retreatment within 4 to 5 weeks after the first treatment. Consult your veterinarian before administering to sick swine. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism. Do not administer within 72 hours of slaughter for food.

[40 FR 13838, Mar. 27, 1975, as amended at 43 FR 11176, Mar. 17, 1978; 44 FR 59508, Oct. 16, 1979; 44 FR 72586, Dec. 14, 1979; 46 FR 25085, May 5, 1981; 52 FR 20598, June 2, 1987]

§ 520.1242b Levamisole hydrochloride tablet or oblet (bolus).

(a) *Chemical name.* (-)-2,3,5,6-Tetrahydro-6-phenylimidazo [2,1-b] thiazole monohydrochloride.

(b) *Specifications.* Assay of not less than 98 percent by nonaqueous titration with 0.1 N potassium isopropoxide; 1 isomer minimum 95 percent pure by optical rotation.

(c) *Sponsor.* See Nos. 011716 and 043781 in § 510.600(c) of this chapter.

(d) *Required labeling.* Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

(e) *Related tolerances.* See § 556.350 of this chapter.

(f) *Conditions of use.* (1) It is used in an oblet for cattle as follows:

(i) *Amount.* 2.19 grams per oblet.

(ii) *Indications for use.* Anthelmintic effective against the following nematode infections: Stomach worms (*Haemonchus*, *Trichostrongylus*, *Ostertagia*), intestinal worms (*Trichostrongylus*, *Cooperia*, *Nematodirus*, *Bunostomum*, *Oesophagostomum*), and lungworms (*Dictyocaulus*).

(iii) *Limitations.* Administer as a single dose as follows: 250 to 450 pounds, ½ oblet; 450 to 750 pounds, 1 oblet; and 750 to 1,050 pounds, 1½ oblets; conditions of constant helminth exposure may require re-treatment within 2 to 4 weeks after the first treatment; do not slaughter for food within 48 hours of treatment; not for use in dairy animals of breeding

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age; consult veterinarian before using in severely debilitated animals.

(2) It is used in a tablet for sheep as follows:

(i) *Amount.* 0.184 gram per tablet.

(ii) *Indications for use.* Anthelmintic effective against the following nematode infections: Stomach worms (*Haemonchus*, *Trichostrongylus*, *Ostertagia*), intestinal worms (*Trichostrongylus*, *Cooperia*, *Nematodirus*, *Bunostomum*, *Oesophagostomum*, *Chabertia*), and lungworms (*Dictyocaulus*).

(iii) *Limitations.* Administer one tablet for each 50 pounds of body weight; conditions of constant helminth exposure may require re-treatment within 2 to 4 weeks after the first treatment; do not slaughter for food within 72 hours of treatment; consult a veterinarian before using in severely debilitated animals.

[40 FR 13838, Mar. 27, 1975, as amended at 44 FR 59507, Oct. 16, 1979]

§ 520.1242c Levamisole hydrochloride and piperazine dihydrochloride.

(a) *Specifications.* (1) The drug is an aqueous solution which contains in each fluid ounce 0.36 gram of levamisole hydrochloride and piperazine dihydrochloride equivalent to 3.98 grams of piperazine base.

(2) The drug is a soluble powder which when reconstituted with water contains in each fluid ounce 0.45 gram of levamisole hydrochloride and piperazine dihydrochloride equivalent to 5.0 grams of piperazine base.

(b) *Sponsor.* See No. 043781 in § 510.600(c) of this chapter.

(c) [Reserved]

(d) *Conditions of use.* It is used as a drench for horses as follows:

(1) *Indications for use.* An anthelmintic effective against infections of large strongyles (*Strongylus vulgaris*, *S. edentatus*), small strongyles (*Cylicocercus* spp., *Cylicocylcus* spp., *Cylicodontophorus* spp., *Cylicostephanus* spp., *Cylicotetrapedon* spp.), ascarids (*Parascaris equorum*), and pinworms (*Oxyuris equi*).

(2) *Limitations.* Aqueous solution: administer by stomach tube or drench 1 fluid ounce per 100 pounds of body weight. Reconstituted soluble powder: administer by stomach tube 1 fluid

ounce per 125 pounds of body weight. If reinfection occurs, re-treat animals at 6- to 8-week intervals. Do not treat animals intended for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 32831, Aug. 5, 1975, as amended at 41 FR 48731, Nov. 5, 1976; 43 FR 11176 Mar. 17, 1978]

§ 520.1242d Levamisole resinates.

(a) *Specifications.* The drug is levamisole adsorbed on a resin, in a concentration equivalent to 10 percent levamisole hydrochloride. Each 2.05-ounce (58.1 gram) packet contains levamisole equivalent to 5.806 grams of levamisole hydrochloride.

(b) *Sponsor.* See No. 043781 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See § 556.350 of this chapter.

(d) *Conditions of use.* In swine it is used as follows:

(1) *Amount.* The equivalent of 8 milligrams per kilogram of body weight, as a single dose, mixed in the animal's ration.

(2) *Indications for use.* For the removal of and control of the following nematode infections: large roundworms (*Ascaris suum*), nodular worms (*Oesophagostomum* spp.), lungworms (*Melastrogylus* spp.), intestinal threadworms (*Strongyloides ransomi*), and swine kidney worms (*Stephanurus dentatum*).

(3) *Limitations.* For pigs from weaning to market weight, mix one 58.1-gram packet of levamisole resinates containing the equivalent of 10-percent levamisole hydrochloride in 40 pounds of feed and administer 1 pound of medicated feed per 40 pounds of body weight as sole ration. For breeding swine, mix 1 packet of the 10-percent resinates in 16 pounds of feed and administer 1 pound of medicated feed per 100 pounds of body weight as sole ration. Administer as single doses. Withhold regular feed overnight and administer medicated feed the following morning. Do not withhold water during fasting. Do not treat within 72 hours of slaughter. Salivation or muzzle foam may be observed. The reaction will disappear a short time after feeding. If pigs are infected with mature lungworms, coughing and vom-

iting may be observed. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

[43 FR 18171, Apr. 28, 1978, as amended at 45 FR 3574, Jan. 18, 1980]

§ 520.1242e Levamisole hydrochloride effervescent tablets.

(a) *Specifications.* Each tablet contains 907 milligrams of levamisole hydrochloride.

(b) *Sponsor.* See No. 043781 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See § 556.350 of this chapter.

(d) *Conditions of use.* It is used for swine as follows:

(1) *Amount.* The equivalent of 8 milligrams of levamisole hydrochloride per kilogram of body weight, as a single dose.

(2) *Indications for use.* See § 520.1242a(f)(3)(ii).

(3) *Limitations.* Withholding water from pigs before treatment is not necessary. Add one tablet for each 2½ gallons of water; mix thoroughly. Allow 1 gallon of medicated water for each 100 pounds body weight of pigs to be treated. No other source of water should be offered. After pigs have consumed medicated water, resume use of regular water. Pigs maintained under conditions of constant worm exposure may require re-treatment within 4 to 5 weeks. Consult your veterinarian before administering to sick swine. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism. Do not administer within 72 hours of slaughter for food.

[45 FR 6087, Jan. 25, 1980]

§ 520.1242f Levamisole hydrochloride gel.

(a) *Specifications.* The drug is a gel containing 11.5 percent levamisole hydrochloride.

(b) *Sponsor.* See No. 043781 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See § 556.350 of this chapter.

(d) *Conditions of use—(1) Cattle—(i) Amount.* Eight milligrams of levamisole hydrochloride per kilogram of body weight, as a single oral dose.

(ii) *Indications for use.* Anthelmintic effective against the following nematode infections: Stomach worms (*Haemonchus*, *Trichostrongylus*, *Ostertagia*), intestinal worms (*Trichostrongylus*, *Cooperia*, *Nematodirus*, *Bunostomum*, *Oesophagostomum*), and lungworms (*Dictyocaulus*).

(iii) *Limitations.* Conditions of constant helminth exposure may require re-treatment within 2 to 4 weeks after the first treatment; do not administer to cattle within 6 days of slaughter for food; do not administer to dairy animals of breeding age; consult veterinarian before using in severely debilitated animals.

(2) *Breeding swine*—(i) *Amount.* Eight milligrams per kilogram of body weight (3.6 milligrams per pound) as a single oral dose.

(ii) *Conditions of use.* For treating breeding swine infected with the following nematodes: Large roundworms (*Ascaris suum*), nodular worms (*Oesophagostomum* spp.), lungworms (*Metastrongylus* spp.), intestinal threadworms (*Strongyloides ransomi*), and kidney worms (*Stephanurus dentatus*).

(iii) *Limitations.* May require re-treatment in 4 to 5 weeks. Do not use within 11 days of slaughter for food. Consult your veterinarian for assistance before using in severely debilitated animals and in the diagnosis, treatment, and control of parasitism.

[47 FR 22517, May 25, 1982; 47 FR 30242, July 13, 1982, as amended at 48 FR 11429, Mar. 18, 1983; 51 FR 29215, Aug. 15, 1986]

§ 520.1242g Levamisole resinates and famphur paste.

(a) *Chemical name of famphur.* O, O-Dimethyl O-[p-(dimethylsulfamoyl) phenyl] phosphorothioate.

(b) *Specifications.* The drug is a paste containing 11.6 percent levamisole resinates (50 percent potency) and 23.6 percent famphur.

(c) *Sponsor.* See 010042 in § 510.600(c) of this chapter.

(d) *Special considerations.* Do not use any cholinesterase-inhibiting drugs, pesticides, insecticides, or chemicals on cattle simultaneously or within a few days before or after treatment with this product.

(e) *Related tolerances.* See § 556.350 of this chapter for levamisole and 40

CFR 180.233 (under the chemical name) for famphur.

(f) *Conditions of use in cattle*—(1) *Amount.* 8 milligrams of levamisole hydrochloride (equivalent) and 30 milligrams of famphur activity per kilogram of body weight.

(2) *Indications for use.* For treatment of cattle infected with the following parasites: Stomach worms (*Haemonchus*, *Trichostrongylus*, *Ostertagia*), intestinal worms (*Trichostrongylus*, *Cooperia*, *Nematodirus*, *Bunostomum*, *Oesophagostomum*), lungworms (*Dictyocaulus*), cattle grubs (*Hypoderma*), biting lice (*Bovicola*), and sucking lice (*Linognathus*, *Solenopotes*).

(3) *Limitations.* Drug is not effective against lice eggs. Conditions of constant helminth and ectoparasitic exposure may require retreatment within 2 to 4 weeks after first treatment. Do not administer to cattle within 19 days of slaughter. Do not administer to dairy animals of breeding age. Do not use in calves less than 3 months old, or in debilitated animals. Do not treat Brahman bulls. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

[53 FR 23757, June 24, 1988, as amended at 54 FR 1353, Jan. 13, 1989]

§ 520.1263 Lincomycin hydrochloride monohydrate oral dosage forms.

§ 520.1263a Lincomycin hydrochloride monohydrate tablets and sirup.

(a) *Specifications.* The lincomycin hydrochloride monohydrate of the tablet meets the specifications prescribed by § 453.30(a)(1) of this chapter. The sirup meets the specifications prescribed by § 453.130b(a)(1) of this chapter.

(b) *Sponsor.* See No. 000009 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is indicated in infections caused by gram-positive organisms which are sensitive to its action, particularly streptococci and staphylococci.

(2) It is administered orally to dogs and cats at a dosage level of 10 mgs per pound of body weight every 12 hours, or 7 mgs per pound of body weight every 8 hours. Treatment may

be continued for periods as long as 12 days if clinical judgment indicates.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13838, Mar. 27, 1975, as amended at 44 FR 7130, Feb. 6, 1979]

§ 520.1263b Lincomycin hydrochloride monohydrate and spectinomycin sulfate tetrahydrate soluble powder.

(a) *Specifications.* The lincomycin hydrochloride monohydrate meets the specifications prescribed by § 463.30(a)(1) of this chapter. The spectinomycin sulfate tetrahydrate used in manufacturing the drug is the antibiotic substance produced by the growth of *Streptomyces spectabilis* or the same antibiotic substance produced by any other means. The quantity of total antibiotic activity cited in this section refers to the equivalent weight of the base activity of the drugs. Lincomycin hydrochloride monohydrate and spectinomycin sulfate tetrahydrate are present in the drug in the ratio of 1 to 2 on the basis of equivalency of lincomycin base to equivalency of spectinomycin base.

(b) *Sponsor.* See No. 000009 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See §§ 556.600 and 556.360 of this chapter.

(d) *Conditions of use.* (1) It is administered in the drinking water of chickens up to 7 days of age as an aid in the control of airsacculitis caused by either *Mycoplasma synoviae* or *Mycoplasma gallisepticum* susceptible to lincomycin-spectinomycin and complicated chronic respiratory disease (air sac infection) caused by *Escherichia coli* and *M. gallisepticum* susceptible to lincomycin-spectinomycin.

(2) For aid in the control of these conditions it is administered in the drinking water at a level of 2 grams of antibiotic activity per gallon of water as the sole source of water for the first 5 to 7 days of life.

[40 FR 13838, Mar. 27, 1975, as amended at 41 FR 1891, Jan. 13, 1976]

§ 520.1263c Lincomycin hydrochloride soluble powder.

(a) *Specifications.* Each 1.41 ounce packet (40 grams) contains 16 grams of lincomycin hydrochloride.

(b) *Sponsor.* See No. 000009 in § 510.600(c) of this chapter.

(c) *Tolerances.* See § 556.360 of this chapter.

(d) *Conditions of use.* (1) *Amount.* 250 milligrams per gallon of drinking water.

(2) *Dosage.* 3.8 milligrams per pound of body weight per day.

(3) *Indications for use.* Treatment of swine dysentery (bloody scours).

(4) *Limitations.* Discard medicated drinking water if not used within 2 days. Prepare fresh stock solution daily. Do not use for more than 10 days. If clinical signs of disease have not improved within 6 days, discontinue treatment and reevaluate diagnosis. Not for use in swine weighing more than 250 pounds. Do not slaughter swine for 6 days following last treatment.

[48 FR 3966, Jan. 28, 1983]

§ 520.1284 Sodium liothyronine tablets.

(a) *Specifications.* Sodium liothyronine tablets consist of tablets intended for oral administration which contain liothyronine at 60 or 120 micrograms per tablet, as the sodium salt.

(b) *Sponsor.* See No. 011519 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is indicated in cases of hypothyroidism in dogs.

(2) It is administered orally to dogs at levels up to 12.8 micrograms per kilogram of body weight per day. Dosage should be adjusted according to the severity of the condition and the response of the patient. Dosage at the total replacement level (12.8 µg per kilogram of body weight) should be considered for initiating therapy and then titrated downward for optimum maintenance effect. Twice daily administration is recommended.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

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§ 520.1320 Mebendazole oral.

(a) *Chemical name.* Methyl 5-benzoyl-benzimidazole-2-carbamate.

(b) *Specifications.* As oral powder: Each gram contains either 40 or 166.7 milligrams of mebendazole. As oral paste: Each gram contains 200 milligrams of mebendazole. As oral suspension: Each milliliter contains 33.3 milligrams of mebendazole.

(c) *Sponsor.* See No. 011716 in § 510.600(c) of this chapter.

(d) *Conditions of use—(1) Horses—(i) Amount.* 1 gram of mebendazole per 250 pounds of body weight per dose, as an oral powder, paste or suspension.

(ii) *Indications for use.* It is used in horses for treatment of infections caused by large roundworms (*Parascaris equorum*); large strongyles (*Strongylus edentatus*, *S. equinus*, *S. vulgaris*); small strongyles; and mature and immature (4th larval stage pinworms (*Oxyuris equi*)).

(iii) *Limitations—(a) Oral powder.* The drug is given by sprinkling directly on the grain portion of the ration or dissolving in 2 to 4 pints of water and administering by stomach tube. The drug is compatible with carbon disulfide, which can be used concurrently for both control (*Gastrophilus* spp.). Routine cautions regarding the use of carbon disulfide must be observed. Do not administer to horses intended for use as food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(b) *Oral paste.* The drug is given by dosing gun (syringe), inserting the tip of the gun at the interdental space in the horse's mouth and depositing the paste on the animal's tongue. The hand is placed under the animal's jaw, and the head is raised to assure that the paste is deposited on the roof of the mouth. Not for use in horses intended for food. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

(c) *Oral suspension.* The drug is administered by stomach tube. Not for horses intended for food use. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(2) *Dogs—(i) Amount.* One hundred milligrams of mebendazole per 10 pounds of body weight, once daily for 3 days, as an oral powder.

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(ii) *Indications for use.* The drug is used for treatment of infections of roundworms (*Toxocara canis*), hookworms (*Ancylostoma caninum*, *Uncinaria stenocephala*), whipworms (*Trichuris vulpis*), and tapeworms (*Taenia pisiformis*).

(iii) *Limitations.* Administer as an oral powder by mixing with a small quantity of food, preferably before the regular meal. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[42 FR 61255, Dec. 2, 1977, as amended at 43 FR 35686, Aug. 11, 1978; 45 FR 3574, Jan. 18, 1980; 46 FR 47218, Sept. 25, 1981; 46 FR 53658, Oct. 30, 1981]

§ 520.1326 Mebendazole and trichlorfon oral dosage forms.

§ 520.1326a Mebendazole and trichlorfon powder.

(a) *Specifications.* Each gram of powder contains 83.3 milligrams of mebendazole and 375.0 milligrams of trichlorofon.

(b) *Sponsor.* See No. 011716 in § 510.600(c) of this chapter.

(c) *Conditions of use—Horses—(1) Amount.* 8.8 milligrams of mebendazole and 40 milligrams of trichlorofon per kilogram of body weight.

(2) *Indications for use.* It is used in horses for the treatment of infections of bots (*Gastrophilus intestinalis* and *G. nasalis*), large roundworms (*Parascaris equorum*), large strongyles (*Strongylus edentatus*, *S. equinus*, *S. vulgaris*), small strongyles, and pinworms (*Oxyuris equi*).

(3) *Limitations.* Administer orally as an individual dose by stomach tube or thoroughly mixed in the ground grain portion of the ration to be consumed in one feeding. Discard treated feed not consumed. Do not administer more than once every 30 days. Do not treat sick or debilitated animals, foals under 4 months of age, or mares in the last month of pregnancy. Trichlorofon is a cholinesterase inhibitor. Do not administer simultaneously or within a few days before or after treatment with, or exposure to, cholinesterase-inhibiting drugs, pesticides or chemicals. Do not administer intravenous anesthetics, especially muscle relaxants concurrently. Not for horses intended

for food use. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[45 FR 10759, Feb. 19, 1980, as amended at 46 FR 52330, Oct. 27, 1981. Redesignated at 51 FR 13212, Apr. 18, 1986]

§ 520.1326b Mebendazole and trichlorfon paste.

(a) *Specifications.* Each gram of paste contains 100 milligrams of mebendazole and 454 milligrams of trichlorfon.

(b) *Sponsor.* See No. 011716 in § 510.600(c) of this chapter.

(c) *Conditions of use.*—(1) *Amount.* 8.8 milligrams of mebendazole and 40 milligrams of trichlorfon per kilogram of body weight.

(2) *Indications for use.* It is used in horses for treatment of infections of bots (*Gastrophilus intestinalis* and *G. assalis*), large roundworms (*Parascaris equorum*), large strongyles (*Strongylus edentatus*, *S. equinus*, *S. vulgaris*), small strongyles, and pinworms (*Oxyuris equi*).

(3) *Limitations.* Do not administer more than once every 30 days. Do not treat sick or debilitated animals, foals under 4 months of age, or mares in the last month of pregnancy. Trichlorfon is a cholinesterase inhibitor. Do not administer simultaneously or within a few days before or after treatment with, or exposure to, cholinesterase-inhibiting drugs, pesticides, or chemicals. Do not administer intravenous anesthetics, especially muscle relaxants, concurrently. Not for use in horses intended for food. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

[51 FR 13212, Apr. 18, 1986]

§ 520.1330 Meclofenamic acid granules.

(a) *Chemical name.* N-(2,6-Dichlorom-tolyl) anthranilic acid.

(b) *Specifications.* The drug is in granular form containing 5 percent meclofenamic acid.

(c) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(d) *Conditions of use.* (1) The drug is used in horses for the treatment of acute or chronic inflammatory dis-

eases involving the musculoskeletal system.

(2) It is administered orally at a dosage of 1 milligram per pound of body weight (1 gram per 1,000 pounds) once daily for 5 to 7 days by addition to the daily grain ration.

(3) Treatment beyond the initial 5- to 7-day period may be indicated. A maintenance dosage level should be individualized for each animal.

(4) This drug should not be administered to horses with active gastrointestinal hepatic, or renal disease.

(5) Not for use in horses intended for food.

(6) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[41 FR 5632, Feb. 9, 1976, as amended at 53 FR 23390, June 22, 1988]

§ 520.1331 Meclofenamic acid tablets.

(a) *Specifications.* Each tablet contains either 10 or 20 milligrams of meclofenamic acid.

(b) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(c) *Conditions of use in dogs.*—(1) *Amount.* 1.1 milligrams per kilogram (0.5 milligram per pound) daily for 5 to 7 days.

(2) *Indications for use.* For the relief of signs and symptoms of chronic inflammatory disease involving the musculoskeletal system.

(3) *Limitations.* For oral use only. Should not be administered to animals with congestive heart failure or active gastrointestinal, hepatic, or renal disease. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[50 FR 43385, Oct. 25, 1985, as amended at 53 FR 23390, June 22, 1988]

§ 520.1341 Megestrol acetate tablets.

(a) *Specifications.* Each tablet contains 5 or 20 milligrams of megestrol acetate.

(b) *Sponsor.* No. 000061 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used in female dogs for the postponement of estrus and the alleviation of false pregnancy.

(2) It is administered orally, intact, or crushed and mixed with food as follows:

(i) For the postponement of estrus by proestrus treatment, 1 milligram per pound of body weight per day for 8 days.

(ii) For the postponement of estrus by anestrus treatment, 0.25 milligram per pound of body weight per day for 32 days.

(iii) For alleviation of false pregnancy, 1 milligram per pound of body weight per day for 8 days.

(3) Full dosage regimen must be completed to produce the desired effect.

(4) Examination of vaginal smears is recommended to confirm detection of proestrus.

(5) Do not administer for more than two consecutive treatments.

(6) Once therapy is started, the animal should be confined for 3 to 8 days or until cessation of bleeding, since dogs in proestrus accept a male.

(7) Do not use prior to or during first estrus cycle.

(8) Do not use in pregnant animals.

(9) Do not use in the presence of a disease of the reproductive system or with mammary tumors.

(10) Should estrus occur within 30 days after cessation of treatment, mating should be prevented.

(11) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13838, Mar. 27, 1975, as amended at 52 FR 7832, Mar. 13, 1987]

§ 520.1380 Methocarbamol tablets.

(a) *Chemical name.* 3-(O-Methoxyphenoxy)-1,2-propanediol 1-carbamate.

(b) *Specifications.* Each tablet contains 500 milligrams of methocarbamol.

(c) *Sponsor.* See No. 000031 in § 510.600(c) of this chapter.

(d) *Conditions of use.* (1) The drug is administered to dogs and cats as an adjunct to therapy for acute inflammatory and traumatic conditions of the skeletal muscles in order to reduce muscular spasms.

(2) Dosage is based upon severity of symptoms and response noted. The usual initial dose is 60 milligrams per pound of body weight in two or three

equally divided doses followed by 30 to 60 milligrams per pound of body weight each following day, usually not to exceed 14 to 21 days.

(3) For use only by or on the order of a licensed veterinarian.

§ 520.1408 Methylprednisolone tablets.

(a) *Specifications.* Each tablet contains 1, 2, or 4 milligrams of methylprednisolone.

(b) *Sponsor.* See No. 000009 in § 510.600(c) of this chapter for use of 1- and 4-milligram tablets; see No. 054273 for use of 1- and 2-milligram tablets.

(c) *NAS/NRC status.* The conditions of use have been NAS/NRC reviewed and found effective. NADA's for approval of drugs for these conditions of use need not include effectiveness data specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(d) *Special consideration.* (1) Clinical and experimental data have demonstrated that corticosteroids administered orally or parenterally to animals may induce the first stage of parturition when administered during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis.

(2) Systemic therapy with methylprednisolone is contraindicated in animals with arrested tuberculosis, peptic ulcer, acute psychoses, or cushingoid syndrome. The presence of active tuberculosis, diabetes, osteoporosis, chronic psychotic reactions, predisposition to thrombophlebitis, hypertension, congestive heart failure, or renal insufficiency necessitates carefully controlled use of corticosteroids. Some of these conditions occur only rarely in dogs and cats but should be kept in mind.

(3) Anti-inflammatory action of corticosteroids may mask signs of infection.

(e) *Conditions of use—(1) Amount.* Dogs and cats: 5 to 15 pounds, 2 milligrams; 15 to 40 pounds, 2 to 4 milligrams; 40 to 80 pounds, 4 to 8 milligrams.

(2) *Indications for use.* For use in dogs and cats as an anti-inflammatory agent.

(3) *Limitations.* Administer total daily dose orally in equally divided doses 6 to 10 hours apart until response is noted or 7 days have elapsed. When response is attained, dosage should be gradually reduced until maintenance level is achieved. Hazardous for human use. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[47 FR 52697, Nov. 23, 1982, as amended at 49 FR 20810, May 17, 1984; 50 FR 32844, Aug. 15, 1985; 53 FR 40727, Oct. 18, 1988]

§ 520.1409 Methylprednisolone, aspirin tablets.

(a) *Specifications.* Each tablet contains 0.5 milligram of methylprednisolone and 300 milligrams of aspirin.

(b) *Sponsor.* See No. 000009 in § 510.600(c) of this chapter.

(c) *NAS/NRC status.* The conditions of use have been NAS/NRC reviewed and found effective. New animal drug applications for approval of drugs for these conditions of use need not include effectiveness data specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(d) *Special considerations.* (1) Clinical and experimental data have demonstrated that corticosteroids administered orally or parenterally to animals may induce the first stage of parturition when administered during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis.

(2) Systemic therapy with methylprednisolone is contraindicated in animals with tuberculosis, chronic nephritis, peptic ulcer, or Cushingoid syndrome. The presence of diabetes mellitus, osteoporosis, predisposition to thrombophlebitis, hypertension, congestive heart failure, or renal insufficiency necessitates carefully controlled use of corticosteroids.

(3) Anti-inflammatory action of corticosteroids may mask signs of infection.

(e) *Conditions of use—(1) Amount.* Dogs under 15 pounds, $\frac{1}{4}$ to 1 tablet daily; 15 to 60 pounds, 1 to 2 tablets

daily; 60 pounds and over, 2 tablets daily.

(2) *Indications for use.* As an anti-inflammatory and analgesic agent in dogs.

(3) *Limitations.* Administer total daily dose in divided doses 6 to 10 hours apart, with a light feeding. When response is attained, dosage should be gradually reduced until maintenance level is achieved. Do not administer to cats. Do not overdose. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[48 FR 21566, May 13, 1983]

§ 520.1422 Metoserbate hydrochloride.

(a) *Chemical name.* Methyl-*o*-methyl-18-epireserbate hydrochloride.

(b) *Sponsor.* See No. 000003 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See § 556.410 of this chapter.

(d) *Conditions of use.* It is used in drinking water for replacement chickens as follows:

(1) *Amount.* 568.5 milligrams per gallon (0.015 percent).

(i) *Indications for use.* As a tranquilizer for flock treatment of chickens prior to handling.

(ii) *Limitations.* To be used one time as a treatment for replacement chickens up to 16 weeks of age; usual drinking water should be withheld prior to treatment to provide adequate consumption of medicated drinking water; not for use in laying chickens; chickens slaughtered within 72 hours following treatment must not be used for food.

(2) *Amount.* 2 to 4 milligrams per 2.2 pounds of body weight.

(i) *Indications for use.* As an aid in control of hysteria.

(ii) *Limitations.* To be used as a treatment for replacement chickens up to 16 weeks of age; usual drinking water should be withheld prior to treatment to provide adequate consumption of medicated drinking water; the drug should be administered at a dosage level of 4 milligrams per 2.2 pounds of body weight followed by 2 treatments at 4-day intervals of 2 milligrams per 2.2 pounds of body weight; not for use in laying chickens; chick-

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ens slaughtered within 72 hours following treatment must not be used for food.

§ 520.1430 Mibolerone.

(a) *Specifications.* Each milliliter contains 100 micrograms of mibolerone.

(b) *Sponsor.* See No. 000009 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* 30 micrograms for animals weighing 1 to 25 pounds; 60 micrograms for animals weighing 26 to 50 pounds; 120 micrograms for animals weighing 51 to 100 pounds; 180 micrograms for animals weighing over 100 pounds, German Shepherds, or German Shepherd mix.

(2) *Indications for use.* For the prevention of estrus (heat) in adult female dogs not intended primarily for breeding purposes.

(3) *Limitations.* Administer daily, orally or in a small amount of food, at least 30 days before expected initiation of heat, and continue daily as long as desired, but not for more than 24 months. Mibolerone should not be used in bitches before the first estrous period. It is not intended for animals being used primarily for breeding purposes. Use orally in adult female dogs only. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[43 FR 15625, Apr. 14, 1978]

§ 520.1448 Monensin oral dosage forms.

[47 FR 5408, Feb. 5, 1982]

§ 520.1448a Monensin blocks.

(a)(1) *Specifications.* Each pound of protein-mineral block contains 400 milligrams of monensin (0.088 percent) as monensin sodium.

(2) *Sponsor.* See 050112 in § 510.600(c) of this chapter.

(3) *Related tolerances.* See § 556.420 of this chapter.

(4) *Conditions of use—(i) Amount.* 80 to 200 milligrams of monensin (0.2 to 0.5 pound of block) per head per day.

(ii) *Indications for use.* Increased rate of weight gain.

(iii) *Limitations.* Block to be fed free choice to pasture cattle (slaughter, stocker, feeder, and dairy and beef re-

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placement heifers) weighing more than 400 pounds. Provide at least 1 block per 5 head of cattle. Feed blocks continuously. Do not feed salt or minerals containing salt. Do not allow horses or other equines access to formulations containing monensin (ingestion of monensin by equines has been fatal). The effectiveness of this block in cull cows and bulls has not been established.

(b) [Reserved]

(c)(1) *Specifications.* Each pound of protein block contains 175 milligrams of monensin (0.038 percent) as monensin sodium.

(2) *Sponsor.* See 021676 in § 510.600(c) of this chapter.

(3) *Related tolerances.* See § 556.420 of this chapter.

(4) *Conditions of use—(i) Amount.* 40 to 200 milligrams of monensin (0.25 to 1.13 pounds or 4 to 18 ounces of block) per head per day.

(ii) *Indications for use.* Increased rate of weight gain.

(iii) *Limitations.* Blocks to be fed free choice to pasture cattle (slaughter, stocker, and feeder) weighing more than 400 pounds. Provide at least 1 block per 4 head of cattle. Do not allow cattle access to salt or mineral while being fed this product. Ingestion by cattle of monensin at levels of 600 milligrams per head per day and higher has been fatal. Do not allow horses or other equines access to formulations containing monensin (ingestion of monensin by equines has been fatal). Block's effectiveness in cull cows and bulls has not been established.

(d)(1) *Specifications.* Each pound of block contains 400 milligrams of monensin (0.088 percent) as monensin sodium.

(2) *Sponsor.* See 051267 in § 510.600(c) of this chapter.

(3) *Related tolerances.* See § 556.420 of this chapter.

(4) *Conditions of use—(i) Amount.* 50 to 200 milligrams of monensin (2 to 8 ounces of block) per head per day.

(ii) *Indications for use.* Pasture cattle: Increased rate of weight gain.

(iii) *Limitations.* Blocks to be fed free choice to pasture cattle (slaughter, stocker, feeder, and dairy and beef replacement heifers) weighing more

than 400 pounds. Provide at least one block per five head of cattle. Feed blocks continuously. Do not feed salt or mineral supplements in addition to the blocks. Ingestion by cattle of monensin at levels of 600 milligrams per head per day and higher has been fatal. Do not allow horses or other equines access to formulations containing monensin (ingestion of monensin by equines has been fatal). The effectiveness of this block in cull cows and bulls has not been established.

[46 FR 19466, Mar. 31, 1981, as amended at 46 FR 33029, June 26, 1981; 46 FR 50067, Oct. 9, 1981. Redesignated at 47 FR 5408, Feb. 5, 1982, and amended at 48 FR 30362, July 1, 1983; 49 FR 22073, May 25, 1984; 49 FR 24019, June 11, 1984; 49 FR 44895, Nov. 13, 1984; 50 FR 5385, Feb. 8, 1985; 52 FR 27197, July 20, 1987; 52 FR 30151, Aug. 13, 1987]

§ 520.1448b Monensin-mineral granules.

(a) *Specifications.* Each pound of loose mineral granules contains 810 milligrams of monensin as monensin sodium.

(b) *Sponsor.* See No. 030239 in § 510.600(c) of the chapter.

(c) *Related tolerances.* See § 556.420 of this chapter.

(d) *Conditions of use—(1) Amount.* 50 to 200 milligrams of monensin (1 to 4 ounces of product) per head per day.

(2) *Indications for use.* Increased rate of weight gain.

(3) *Limitations.* Medicated mineral granules to be fed free choice to pasture cattle (slaughter, stocker, feeder, and dairy and beef replacement heifers) weighing more than 400 pounds. Provide enough feeding stations to ensure that all animals have free access at all times. Do not feed additional salt or mineral. Do not mix with grain or other feeds. Monensin is toxic to cattle when consumed at higher than approved levels. Stressed or feed and/or water deprived cattle should be adapted to the pasture and to unmedicated mineral supplement before using the product. Do not allow horses or other equines access to formulations containing monensin (ingestion of monensin by equines has been fatal). Product's effectiveness in cull cows and bulls has not been established.

[47 FR 5408, Feb. 5, 1982, as amended at 50 FR 47725, Nov. 20, 1985]

§ 520.1450 Morantel tartrate oral dosage forms.

[49 FR 47831, Dec. 7, 1984]

§ 520.1450a Morantel tartrate bolus.

(a) *Specifications.* Each bolus contains 2.2 grams morantel tartrate equivalent to 1.3 grams of morantel base.

(b) *Sponsor.* See No. 000069 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See § 556.425 of this chapter.

(d) *Conditions of use—(1) Amount.* One bolus per 500 pounds of body weight (4.4 milligrams per pound of body weight) as a single oral dose. Boluses may be divided in half for more accurate dosing as follows: up to 325 pounds, ½ bolus; 326 to 600 pounds, 1 bolus; 601 to 900 pounds, 1½ boluses; and 901 to 1,200 pounds, 2 boluses.

(2) *Indications for use.* For removal and control of mature gastrointestinal nematode infections of cattle including stomach worms (*Haemonchus* spp., *Ostertagia* spp., *Trichostrongylus* spp.), worms of the small intestine (*Cooperia* spp., *Trichostrongylus* spp., *Nematodirus* spp.), and worms of the large intestine (*Oesophagostomum radiatum*).

(3) *Limitations.* Conditions of constant worm exposure may require retreatment in 2 to 4 weeks. Consult your veterinarian before administering to severely debilitated animals and for assistance in the diagnosis, treatment, and control of parasitism. Do not treat within 14 days of slaughter.

[46 FR 50949, Oct. 16, 1981. Redesignated at 49 FR 47831, Dec. 7, 1984, and amended at 51 FR 9005, Mar. 17, 1986]

§ 520.1450b Morantel tartrate cartridge.

(a) *Specifications.* The drug product consists of a stainless-steel cylinder having both ends closed with polyethylene diffusing discs and containing a morantel tartrate paste. The paste contains 22.7 grams of morantel tartrate equivalent to 13.5 grams of morantel base.

(b) *Sponsor.* See No. 000069 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See § 556.425 of this chapter.

(d) *Conditions of use—(1) Amount.* Grazing cattle: Administer 1 cartridge to each animal at the start of the grazing season.

(2) *Indications for use.* For control of the adult stage of the following gastrointestinal nematode infections in weaned calves and yearling cattle weighing a minimum of 200 pounds: *Ostertagia* spp., *Trichostrongylus axei*, *Cooperia* spp., and *Oesophagostomum radiatum*.

(3) *Limitations.* Administer orally with the dosing gun to all cattle that will be grazing the same pasture. Effectiveness of the drug product is dependent upon continuous control of the gastrointestinal parasites for approximately 90 days following administration. Therefore, treated cattle should not be moved to pastures grazed in the same grazing season/calendar year by untreated cattle. Do not administer to cattle within 106 days of slaughter. Consult your veterinarian before administering to severely debilitated animals and for assistance in the diagnosis, treatment, and control of parasitism.

[49 FR 47831, Dec. 7, 1984, as amended at 51 FR 23415, June 27, 1986; 51 FR 41061, Nov. 13, 1986]

§ 520.1468 Naproxen granules.

(a) *Specifications.* Naproxen granules contain 50 percent naproxen.

(b) *Sponsor.* No. 000033 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Horses.* The drug is used for the relief of inflammation and associated pain and lameness exhibited with arthritis, as well as myositis and other soft tissue diseases of the musculoskeletal system of the horse.

(2)(i) For oral maintenance therapy following initial intravenous dosage, administer 10 milligrams naproxen per kilogram of animal body weight twice daily as top dressing in the animal's feed for up to 14 consecutive days. The initial intravenous dosage is 5 milligrams per kilogram of body weight.

(ii) For oral dosage only, administer 10 milligrams naproxen per kilogram of animal body weight twice daily as a

top dressing in the animal's feed for up to 14 consecutive days.

(3) Not for use in horses intended for food.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[41 FR 14188, Apr. 2, 1976, as amended at 51 FR 24525, July 7, 1986]

§ 520.1520 Niclosamide tablets.

(a) *Chemical name.* 2,5-Dichloro-4-nitrosalicylanilide.

(b) *Specifications.* Niclosamide tablets contain niclosamide in a tablet intended for oral administration.

(c) *Sponsor.* See No. 000859 in § 510.600(c) of this chapter.

(d) *Conditions of use.* (1) The drug is intended for removal of tapeworms from dogs (*Dipylidium caninum*, *Taenia pisiformis*, *Taenia hydatigena*) and cats (*Taenia taeniaeformis*).

(2) The drug is administered orally at the rate of 500 milligrams of niclosamide per 7 pounds of body weight. An overnight fast is recommended. Treatment may be repeated should tapeworm proglottids reappear due to reinfection or underdosing.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

§ 520.1560 Nitrofurantoin oral dosage forms.

[42 FR 19143, Apr. 12, 1977]

§ 520.1560a Nitrofurantoin oral suspension.

(a) *Specifications.* Each milliliter contains 15 milligrams of nitrofurantoin in a 10 percent alcoholic suspending medium.

(b) *Sponsor.* See No. 000149 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Dogs and cats.* 1 milliliter (15 milligrams nitrofurantoin) for each 7½ pounds of body weight every 8 hours.

(i) *Indications for use.* For the treatment of canine tracheobronchitis (kennel cough) complicated by secondary bacterial infection and bacteria

urinary infections due to nitrofurantoin-susceptible organisms.¹

(ii) *Limitations.* For tracheobronchitis, administer for 4 to 7 days. For acute urinary tract infections, administer for 7 to 10 days. For chronic urinary tract infections, administer for 10 to 14 days. When laboratory tests are available, administer for 3 days after sterility of urine is attained. In treating dogs and cats, emesis has been reported. To minimize the effect, administer the drug with food or reduce dosage. In the presence of marked impairment of renal function, administer with care. Safe dosage may be less than that usually recommended. When used for extended periods of time, the drug may cause temporary arrest of spermatogenesis, testicular atrophy, and a corresponding weight loss. This is reversible with withdrawal of the drug. In cases where therapy in excess of 5 days is indicated, appropriate laboratory procedures (clinical chemistry, urinalysis, hematology) should be undertaken to monitor the progress of the patient. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(2) *Horses.* 30 milliliters (450 milligrams nitrofurantoin) for each 225 pounds of body weight initially, then 15 milliliters (225 milligrams) every 8 hours.

(i) *Indications for use.* For the treatment of equine tracheopharyngitis (race track cough) caused by secondary bacterial infection, such as streptococci and *Pseudomonas* spp., urinary tract infections caused by hemolytic streptococci and staphylococci, and *Pseudomonas* spp., sensitive to nitrofurantoin.¹

(ii) *Limitations.* For tracheopharyngitis, administer for 5 days. For bacterial urinary infections, administer for 7 days. When laboratory tests are available, administer for 3 days after sterility of urine is attained. In the presence of marked impairment of renal function, administer with care. Safe dosage may be less than that usually recommended. When used for ex-

tended periods of time, the drug may cause temporary arrest of spermatogenesis, testicular atrophy, and a corresponding weight loss. This is reversible with withdrawal of drug. In cases where therapy in excess of 5 days is indicated, appropriate laboratory procedures (clinical chemistry, urine analysis, hematology) should be undertaken to monitor the progress of the patient. Not for use in horses intended for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[42 FR 19143, Apr. 12, 1977, as amended at 44 FR 67114, Nov. 23, 1979]

§ 520.1560b Nitrofurantoin tablets and boluses.

(a) *Specifications.* Each tablet contains 10 milligrams of nitrofurantoin. Each bolus contains 50 milligrams of nitrofurantoin.

(b) *Sponsor.* No. 000149 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) *Amount.* 2 milligrams per pound of body weight every 8 hours.

(2) *Indications for use.* It is used for the treatment of epizootic canine tracheobronchitis (kennel cough) and bacterial urinary tract infections of dogs and cats (nephritis and cystitis) when due to nitrofurantoin-susceptible organisms.

(3) *Limitations.* For canine tracheobronchitis, treat for 4 to 7 days. For acute urinary tract infections, treat for 7 to 10 days. For chronic urinary tract infections, treat for 10 to 14 days, or longer as needed. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[42 FR 19061, Apr. 15, 1977, as amended at 44 FR 67114, Nov. 23, 1979]

§ 520.1628 Oxfendazole powder and pellets.

(a) *Specifications—(1) Powder for suspension.* Each gram of powder contains 7.57 percent oxfendazole.

(2) *Pellets.* Each gram of pellets contains 6.49 percent oxfendazole.

(b) *Sponsor.* See No. 000033 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* 10 milligrams per kilogram of body weight.

¹These conditions are NA3/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter.

(2) *Indications for use.* The drug is used in horses for removal of the following gastrointestinal worms: Large roundworms (*Parascaris equorum*), mature and immature pinworms (*Oxyuris equi*), large strongyles (*Strongylus edentatus*, *Strongylus vulgaris*, and *Strongylus equinus*), and small strongyles.

(3) *Limitations.*—(i) *Powder for suspension.* For gravity administration via stomach tube or for positive administration via stomach tube and dose syringe. Discard unused portions of suspension after 24 hours. Mix drug according to directions prior to use. Administer drug with caution to sick or debilitated horses. Not for use in horses intended for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(ii) *Pellets.* The drug is given by sprinkling on the grain portion of the ration. Withholding feed or water prior to administration is not necessary. Administer drug with caution to sick or debilitated horses. Not for use in horses intended for food. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

[44 FR 35211, June 19, 1979, as amended at 46 FR 26301, May 12, 1981; 46 FR 60570, Dec. 11, 1981; 49 FR 28549, July 13, 1984]

§ 520.1629 Oxfendazole paste.

(a) *Specifications.* Each gram of paste contains 0.375 gram oxfendazole (37.5 percent).

(b) *Sponsor.* See No. 000033 in § 510.600(c) of this chapter.

(c) *Conditions of use.*—(1) *Amount.* 10 milligrams per kilogram (2.2 pounds) of body weight.

(2) *Indications for use.* The drug is used in horses for removal of the following gastrointestinal worms: Large roundworms (*Parascaris equorum*), mature and 4th stage larvae pinworms (*Oxyuris equi*), large strongyles (*Strongylus edentatus*, *S. vulgaris*, and *S. equinus*), and small strongyles.

(3) *Limitations.* Horses maintained on premises where reinfection is likely to occur should be retreated in 6 to 8 weeks. Withholding feed or water prior to use is unnecessary. Administer drug with caution to sick or debilitated horses. Not for use in horses intended

for food. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

[49 FR 38250, Sept. 28, 1984]

§ 520.1630 Oxfendazole suspension.

(a) *Specifications.* Each milliliter contains 90.6 milligrams oxfendazole (9.06 percent).

(b) *Sponsor.* See No. 000033 in § 510.600(c) of this chapter.

(c) *Conditions of use.*—(1) *Amount.* 10 milligrams per kilogram (2.2 pounds) of body weight.

(2) *Indications for use.* The drug is used in horses for removal of the following gastrointestinal worms: Large roundworms (*Parascaris equorum*), mature and 4th stage larvae pinworms (*Oxyuris equi*), large strongyle (*Strongylus edentatus*, *S. vulgaris*, and *S. equinus*), and small strongyles.

(3) *Limitations.* Administer by stomach tube or dose syringe. Horses maintained on premises where reinfection is likely to occur should be retreated in 6 to 8 weeks. Withholding feed or water prior to use is unnecessary. Administer drug with caution to sick or debilitated horses. Not for use in horses intended for food. If for use by stomach tube: Federal law restricts this drug to use by or on the order of a licensed veterinarian. If for use by dose syringe only: Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

[49 FR 38250, Sept. 28, 1984]

§ 520.1631 Oxfendazole and trichlorfon paste.

(a) *Specifications.* Each gram of paste contains 28.5 milligrams oxfendazole and 454.5 milligrams trichlorfon.

(b) *Sponsor.* See 000033 in § 510.600(c) of this chapter.

(c) *Conditions of use.*—(1) *Amount.* 2.5 milligrams of oxfendazole and 4 milligrams of trichlorfon per kilogram of body weight.

(2) *Indications for use.* The drug is used in horses for removal of bot flies (*Gasterophilus intestinalis*, 2nd and 3rd instars; *G. nasalis*, 3rd instar) and the following gastrointestinal worms: Large roundworms (*Parascaris*

equorum), pinworms (*Oxyuris equi*), adult and 4th stage larvae; large strongyles (*Strongylus edentatus*, *S. vulgaris*, and *S. equinus*); and small strongyles.

(3) *Limitations.* Horses maintained on premises where reinfection is likely to occur should be retreated in 6 to 8 weeks. Withholding feed or water before use is unnecessary. Administer with caution to sick or debilitated horses. Not for use in horses intended for food. Do not administer to mares during the last month of pregnancy. Trichlorfon is a cholinesterase inhibitor. Do not use this product in animals simultaneously with, or within a few days before or after treatment with or exposure to, cholinesterase-inhibiting drugs, pesticides, or chemicals. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

[50 FR 50291, Dec. 10, 1985]

§ 520.1638 Oxibendazole paste.

(a) *Specifications.* The paste contains 22.7 percent oxibendazole.

(b) *Sponsor.* See 011519 in § 510.600(c) of this chapter.

(c) *Conditions of use in horses—(1) Amount.* For uses other than for threadworms (*Strongyloides westeri*), 10 milligrams of oxibendazole per kilogram of body weight; for threadworms (*Strongyloides westeri*), 15 milligrams per kilogram.

(2) *Indications for use.* For removal and control of large strongyles (*Strongylus edentatus*, *S. equinus*, *S. vulgaris*); small strongyles (genera *Cylicostephanus*, *Cylicocyclus*, *Cyathostomum*, *Triodontophorus*, *Cylicodontophorus*, and *Gyalocephalus*); large roundworms (*Parascaris equorum*); pinworms (*Oxyuris equi*) including various larval stages; and threadworms (*Strongyloides westeri*).

(3) *Limitations.* Administer orally by syringe. Horses maintained on premises where reinfection is likely to occur should be re-treated in 6 to 8 weeks. Not for use in horses intended for food. Consult a veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

[46 FR 50948, Oct. 16, 1981, as amended at 47 FR 36418, Aug. 20, 1982]

§ 520.1640 Oxibendazole suspension.

(a) *Specifications.* The suspension contains 10 percent oxibendazole.

(b) *Sponsor.* See 011519 in § 510.600(c) of this chapter.

(c) *Conditions of use in horses—(1) Amount.* For use other than threadworms (*Strongyloides westeri*), 10 milligrams of oxibendazole per kilogram of body weight; for threadworms, 15 milligrams per kilogram of body weight.

(2) *Indications for use.* For removal and control of large strongyles (*Strongylus edentatus*, *S. equinus*, *S. vulgaris*); small strongyles (species of the genera *Cylicostephanus*, *Cylicocyclus*, *Cyathostomum*, *Triodontophorus*, *Cylicodontophorus*, and *Gyalocephalus*); large roundworms (*Parascaris equorum*); pinworms (*Oxyuris equi*) including various larval stages; and threadworms (*Strongyloides westeri*).

(3) *Limitations.* Administer by stomach tube in 3 to 4 pints of warm water, or by top dressing or mixing into a portion of the normal grain ration. Prepare individual doses to ensure that each animal receives the correct amount. Horses maintained on premises where reinfection is likely to occur should be re-treated in 6 to 8 weeks. Not for use in horses intended for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[45 FR 78119, Nov. 28, 1980, as amended at 47 FR 39812, Sept. 10, 1982]

§ 520.1660 Oxytetracycline.

§ 520.1660a Oxytetracycline and carbomycin in combination.

(a) *Specifications.* (1) Oxytetracycline: The antibiotic substance produced by growth of *Streptomyces rimosus* or the same antibiotic substance produced by any other means.

(2) Carbomycin: The antibiotic substance produced by growth of *Streptomyces halstedii* or the same antibiotic substance produced by any other means.

(b) *Sponsor.* See No. 000069 in § 510.600(c) of this chapter.

(c) *Special considerations.* The quantities of oxytetracycline in paragraph (e) of this section refer to the

activity of oxytetracycline hydrochloride and the quantities of carbomycin listed refer to the activity of an appropriate standard.

(d) *Related tolerances.* See §§ 556.110 and 556.500 of this chapter.

(e) *Conditions of use.* It is used as oxytetracycline hydrochloride plus carbomycin base in drinking water of chickens as follows:

(1) *Amount.* 1.0 gram of oxytetracycline and 1.0 gram carbomycin per gallon.

(2) *Indications for use.* As an aid in the prevention and treatment of complicated chronic respiratory disease (air-sac infection) caused by *Mycoplasma gallisepticum* and secondary bacterial organisms associated with chronic respiratory disease such as *E. coli*.

(3) *Limitations.* Administer for not more than 5 days; not for use in chickens producing eggs for human consumption; withdraw 24 hours before slaughter.

§ 520.1660b Oxytetracycline hydrochloride capsules.

(a) *Specifications.* The drug is in capsule form with each capsule containing 125 or 250 milligrams of oxytetracycline hydrochloride. Oxytetracycline is the antibiotic substance produced by growth of *Streptomyces rimosus* or the same antibiotic substance produced by any other means.

(b) *Sponsor.* See No. 000069 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is used in dogs and cats for the treatment of bacterial pneumonia caused by *Brucella bronchiseptica*, tonsillitis caused by *Streptococcus hemolyticus*, bacterial enteritis caused by *Escherichia coli*, urinary tract infections caused by *Escherichia coli*, and wound infections caused by *Staphylococcus aureus*.¹

(2) The drug is administered orally to dogs and cats at a dosage level of 25-50 milligrams per pound of body weight per day in divided doses at 12-hour intervals. The drug can be used

¹ These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

for continuation of compatible antibiotic therapy following parenteral oxytetracycline administration where rapidly attained, sustained antibiotic blood levels are required. The duration of treatment required to obtain favorable response will depend to some extent on the severity and degree of involvement and the susceptibility of the infectious agent. Clinical response to antibiotic therapy usually occurs within 48 to 72 hours. If improvement is not observed within that period, the diagnosis and course of treatment should be reconsidered. To assure adequate treatment, administration of the drug should continue for at least 48 hours following favorable clinical response.¹

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

§ 520.1660c Oxytetracycline hydrochloride tablets.

(a) *Specifications.* Each tablet contains 250 or 500 milligrams of oxytetracycline hydrochloride.

(b) *Sponsor.* See No. 000069 in § 510.600(c) of this chapter.

(c) *NAS/NRC status.* The conditions of use of oxytetracycline hydrochloride in paragraph (e)(2) of this section have been reviewed by NAS/NRC and found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter but may require bioequivalency and safety information.

(d) *Tolerances.* See § 556.500 of this chapter.

(e) *Conditions of use in beef and dairy cattle.*—(1)(i) *Amount.* 250 milligrams per 100 pounds of body weight every 12 hours (5 milligrams per pound of body weight daily in two doses).

(ii) *Indications for use.* For control of bacterial enteritis caused by *Salmonella typhimurium* and *Escherichia coli* (colibacillosis) and bacterial pneumonia (shipping fever complex, pasteurellosis) caused by *Pasteurella multocida*.

(2)(i) *Amount.* 500 milligrams per 100 pound of body weight every 12 hours (10 milligrams per pound of body weight daily in two doses).

(ii) *Indications for use.* For treatment of bacterial enteritis caused by *Salmonella typhimurium* and *Escherichia coli* (colibacillosis) and bacterial pneumonia (shipping fever complex, pasteurellosis) caused by *Pasteurella multocida*.

(3) *Limitations.* Dosage should continue until the animal returns to normal and for 24 hours to 48 hours after symptoms have subsided. Treatment should not exceed 4 consecutive days. Do not exceed 500 milligrams per 100 pounds of body weight every 12 hours (10 milligrams per pound daily). Discontinue treatment 7 days prior to slaughter. Not for use in lactating dairy cattle.

[46 FR 32440, June 23, 1981, as amended at 50 FR 1045, Jan. 9, 1985]

§ 520.1660d Oxytetracycline hydrochloride soluble powder.

(a) *Specifications.* (1) Each 2.46-ounce (70-gram) packet contains 25.6 grams of oxytetracycline hydrochloride.

(2) Each 9.87-ounce (280-gram) packet contains 102.4 grams of oxytetracycline hydrochloride.

(b) *Sponsor.* See No. 017144 in § 510.600(c) of this chapter.

(c) *NAS/NRC status.* The conditions of use specified in paragraph (e) of this section are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified in § 514.111 of this chapter, but may require bioequivalency and safety information.

(d) *Related tolerances.* See § 566.500 of this chapter.

(e) *Conditions of use.* (1) It is used in drinking water as follows:

(i) *Chickens—(A)(1) Amount per gallon.* 200 to 400 milligrams.

(2) *Indications for use.* Control of infectious synovitis caused by *Mycoplasma synoviae* susceptible to oxytetracycline.

(3) *Limitations.* Prepare a fresh solution daily. Administer 7 to 14 days. Not to be used for more than 14 consecutive days. Use as sole source of drinking water. Do not use in birds producing eggs for human consumption.

(B)(1) *Amount per gallon.* 400 to 800 milligrams.

(2) *Indications for use.* Control of chronic respiratory disease (CRD) and air sac infections caused by *Mycoplasma gallisepticum* and *E. coli* susceptible to oxytetracycline; control of fowl cholera caused by *Pasteurella multocida* susceptible to oxytetracycline.

(3) *Limitations.* Prepare a fresh solution daily. Administer 7 to 14 days. Not to be used for more than 14 consecutive days. Use as sole source of drinking water. Do not use in birds producing eggs for human consumption.

(ii) *Turkeys—(A)(1) Amount per gallon.* 200 to 400 milligrams.

(2) *Indications for use.* Control of hexamitiasis caused by *Hexamita meleagridis* susceptible to oxytetracycline.

(3) *Limitations.* Prepare a fresh solution daily. Administer 7 to 14 days. Not to be used for more than 14 consecutive days. Use as sole source of drinking water. Do not use in birds producing eggs for human consumption. Withdraw 5 days prior to slaughter.

(B)(1) *Amount per gallon.* 400 milligrams.

(2) *Indications for use.* Control of infectious synovitis caused by *Mycoplasma synoviae* susceptible to oxytetracycline.

(3) *Limitations.* Prepare a fresh solution daily. Administer 7 to 14 days. Not to be used for more than 14 consecutive days. Use as sole source of drinking water. Do not use in birds producing eggs for human consumption. Withdraw 5 days prior to slaughter.

(C)(1) *Amount.* 25 milligrams per pound of body weight.

(2) *Indications for use.* Growing turkeys. Control of complicating bacterial organisms associated with bluecomb (transmissible enteritis, coronaviral enteritis) susceptible to oxytetracycline.

(3) *Limitations.* Prepare a fresh solution daily. Administer 7 to 14 days. Not to be used for more than 14 consecutive days. Use as sole source of drinking water. Do not use in birds producing eggs for human consumption. Withdraw 5 days prior to slaughter.

(2) [Reserved]

§ 520.1720

[50 FR 32694, Aug. 14, 1985, as amended at 52 FR 48094, Dec. 18, 1987]

§ 520.1720 Phenylbutazone oral dosage forms.

§ 520.1720a Phenylbutazone tablets and boluses.

(a) *Specifications.* Each tablet contains 100, 200, or 400 milligrams, or 1 gram of phenylbutazone. Each bolus contains 2 or 4 grams of phenylbutazone.

(b) *Sponsor.* See sponsor numbers in § 510.600(c) of this chapter, as follows:

(1) No. 017220 for use of 100- or 400-milligram or 1-gram tablets, or 2- or 4-gram boluses, in dogs and horses.

(2) No. 000010 for use of 100- or 200-milligrams or 1-gram tablets in dogs and horses.

(3) Nos. 000031, 000591, 000856, 000864, and 053617 for use of 100-milligram or 1-gram tablets in dogs and horses.

(4) No. 000832 for use of 100-milligram tablets in dogs.

(c) *Conditions of use—(1) Dogs—(i) Amount.* Twenty milligrams per pound of body weight daily.¹

(ii) *Indications for use.* The drug is used for the relief of inflammatory conditions associated with a musculoskeletal system.¹

(iii) *Limitations.* Administer in three divided doses daily. Do not exceed a total daily dose of 800 milligrams regardless of body weight. Administer at a relatively high dosage level for the first 48 hours and then reduce gradually to a maintenance dosage level with the lowest dosage maintained at a level capable of producing the desired clinical response. Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

(2) *Horses—(i) Amount.* One to two grams per 500 pounds weight daily.¹

(ii) *Indications for use.* This drug is used for the relief of inflammatory conditions associated with the musculoskeletal system.¹

(iii) *Limitations.* Do not exceed a daily dosage of 4 grams per day. Administer at a relatively high dosage level for the first 48 hours and then reduce gradually to a maintenance dosage level with the lowest dosage maintained at the level capable of producing the desired clinical response.

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Not for use in animals intended for food purposes. Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

[42 FR 44227, Sept. 2, 1977, as amended at 45 FR 10333, Feb. 15, 1980; 45 FR 14023, Mar. 4, 1980; 46 FR 48642, Oct. 2, 1981; 47 FR 30968, July 16, 1982; 50 FR 49372, Dec. 2, 1985; 52 FR 36023, Sept. 25, 1987]

§ 520.1720b Phenylbutazone granules.

(a) *Specifications.* The drug is in granular form. It is packaged to contain either 8 grams of phenylbutazone per package or 1 gram of phenylbutazone per package.

(b) *Sponsor.* See 017220 in § 510.600(c) for 8-gram package, see 047408 for 1-gram package.

(c) *NAS/NRC status.* The conditions of use have been NAS/NRC reviewed and found effective. NADA's for approval of drugs for these conditions of use need not include effectiveness data, specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(d) *Conditions of use—(1) Horses—(i) Amount.* 1 to 2 grams per 500 pounds of body weight, not to exceed 4 grams, daily, as required.

(ii) *Indications.* For the treatment of inflammatory conditions associated with the musculoskeletal system.

(iii) *Limitations.* Administer orally by adding to a portion of the usual grain ration. Use a relatively high dose for the first 48 hours, then gradually reduce to a maintenance level at the lowest level capable of producing the desired clinical response. Treated animals should not be slaughtered for food use. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[46 FR 18960, Mar. 27, 1981, as amended at 46 FR 48642, Oct. 2, 1981]

§ 520.1720c Phenylbutazone paste.

(a) *Specifications.* The paste contains 20 percent phenylbutazone.

(b) *Sponsor.* See 017220 in § 510.600(c) of this chapter.

(c) *NAS/NRC status.* The conditions of use are NAS/NRC reviewed and found effective. Applications for these

¹ See footnote 1 to § 520.1660b.

uses need not include effectiveness data as specified in § 514.111 of this chapter, but may require bioequivalency and safety information.

(d) *Conditions of use in horses*—(1) *Amount*. 1 to 2 grams of phenylbutazone per 500 pounds of body weight, not to exceed 4 grams daily.

(2) *Indications for use*. For relief of inflammatory conditions associated with the musculoskeletal system.

(3) *Limitations*. Use a relatively high dose for the first 48 hours, then gradually reduce to a maintenance level of the lowest level capable of producing the desired clinical response. Not for use in horses intended for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[45 FR 84762, Dec. 23, 1980]

§ 520.1720d Phenylbutazone gel.

(a) *Specifications*. Each 30 grams of gel contains 4 grams of phenylbutazone.

(b) *Sponsor*. See 053617 in § 510.600(c) of this chapter.

(c) *NAS/NRC status*. The conditions of use are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified in § 514.111 of this chapter, but may require bioequivalency and safety information.

(d) *Conditions of use in horses*—(1) *Amount*. 1 to 2 grams of phenylbutazone per 500 pounds of body weight, not to exceed 4 grams daily.

(2) *Indications for use*. For relief of inflammatory conditions associated with the musculoskeletal system of horses.

(3) *Limitations*. Use a relatively high dose for the first 48 hours, then gradually reduce to a maintenance level at the lowest level capable of producing the desired clinical response. Not for use in horses intended for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[50 FR 13561, Apr. 5, 1985, as amended at 50 FR 49372, Dec. 2, 1985]

§ 520.1760 Phthalofyne tablets.

(a) *Specifications*. Phthalofyne tablets contain 456 milligrams, 912 milli-

grams, and 2.28 grams of phthalofyne.

(b) *Sponsor*. See No. 011716 in § 510.600(c) of this chapter.

(c) *Conditions of use*. (1) The drug is used for the treatment of whipworm (*Trichuris vulpis*) infection in dogs.

(2) It is recommended that dogs be fasted 24 hours prior to a single dose. The drug is administered at a level of one tablet of 456 milligrams per 5 pounds of body weight, one tablet of 912 milligrams per 10 pounds of body weight or one tablet of 2.28 grams per 25 pounds of body weight. An alternative procedure of two doses each administered following light meals in morning and evening is recommended in obstinate cases. The same schedule, noted above, is used for each dose.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13838, Mar. 27, 1975, as amended at 45 FR 31304, May 13, 1980]

§ 520.1780 Piperacetazine tablets.

(a) *Specifications*. Each tablet contains 1 milligram of piperacetazine.

(b) *Sponsor*. See No. 011716 in § 510.600(c) of this chapter.

(c) *Conditions of use*. (1) It is used in dogs and cats as a tranquilizer, sedative, and antiemetic agent and for the symptomatic relief of pruritis.

(2) *Method of administration*:

(i) *Tranquilization*. It is administered initially at the recommended average dosage level of 0.5 milligram per 10 pounds of body weight (1 tablet for every 20 pounds) repeated at 6- to 12-hour intervals for tranquilizing effect. Subsequent doses and the intervals between them may be adjusted as indicated.

(ii) *Sedation*. When sedation is desired, the drug is administered at a dosage level of 1 milligram (1 tablet) per 5 to 10 pounds of body weight. The tablets may be used as supportive therapy following use of the drug in injectable form.

(3) It is not to be used in conjunction with organophosphates and/or procaine hydrochloride, because phenothiazines may potentiate the toxicity of organophosphates and the activity of procaine hydrochloride.

§ 520.1801a

(4) For use only by or on the order of a licensed veterinarian.

§ 520.1801 Piperazine adipate oral dosage forms.

§ 520.1801a Piperazine adipate powder.

(a) *Specifications.* The drug contains a minimum of 98.5 percent piperazine adipate (37 percent piperazine base).

(b) *NAS/NRC status.* The conditions of use specified in this section have been reviewed by NAS/NRC and are effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter.

(c) *Special considerations.* Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

(d) [Reserved]

(e)(1) *Sponsor.* See No. 023851 in § 510.600(c) of this chapter.

(2) *Conditions of use: Dogs*—(i) *Amount.* 1 level ¼ teaspoon scoop (860 milligrams of piperazine adipate) for each 11 pounds of body weight (28.9 milligrams of piperazine base per pound of body weight).

(ii) *Indications for use.* Removal of large roundworms (*Toxocara canis* and *Toxascaris leonina*) from dogs and puppies.

(iii) *Limitations.* Administer by mixing prescribed amount with ½ of the normal ration. A repeat treatment should be given in 10 to 20 days to remove immature roundworms which may have entered the intestine from the lungs after the first dose. Laboratory fecal examinations should always be done to determine the need for treatment.

[44 FR 59509, Oct. 16, 1979. Redesignated at 45 FR 44625, July 1, 1980 and amended at 54 FR 1163, Jan. 12, 1989]

§ 520.1802 Piperazine-carbon disulfide complex oral dosage forms.

§ 520.1802a Piperazine-carbon disulfide complex suspension.

(a) *Specifications.* Each fluid ounce of suspension contains 7.5 grams of piperazine-carbon disulfide complex. The piperazine-carbon disulfide complex contains equimolar parts of piperazine and carbon disulfide (1 gram

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contains 530 mgs of piperazine and 470 mgs of carbon disulfide).

(b) *Sponsor.* See 000009 in § 510.600(c) of this chapter.

(c) *Conditions of use: Horses and ponies*—(1) *Amount.* One fluid ounce per 100 pounds of body weight.¹

(2) *Indications for use.* For removing ascarids (large roundworms, *Parascaris equorum*), bots (*Gastrophilus* spp.), small strongyles, large strongyles (*Strongyles* spp.), and pinworms (*Oxyuris equi*).¹

(3) *Limitations.* Administer by stomach tube or dose syringe after withholding feed overnight or for 8 to 10 hours. Provide water as usual. Resume regular feeding 4 to 6 hours after treatment. Treatment of debilitated or anemic animals is contraindicated. Do not administer to animals that are or were recently affected with colic, diarrhea, or infected with a serious infectious disease. As with most anthelmintics, drastic cathartics and other gastrointestinal irritants should not be administered in conjunction with this drug. Animals in poor condition or heavily parasitized should be given one half the recommended dose and treated again in 2 or 3 weeks. Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

[45 FR 52781, Aug. 8, 1980]

§ 520.1802b Piperazine-carbon disulfide complex boluses.

(a) *Specifications.* Each bolus contains 20 grams of piperazine-carbon disulfide complex.

(b) *Sponsor.* See 000009 in § 510.600(c) of this chapter.

(c) *Conditions of use: Horses and ponies*—(1) *Amount.* For removal of ascarids and small strongyles, 1 bolus (20 grams) per 500 pounds body weight; removal of large strongyles, pinworms, and bots, 1 bolus per 250 pounds body weight.¹

(2) *Indications for use.* For removing ascarids (large roundworms, *Para-*

¹ These conditions are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

Strongylus equorum), large strongyles (*Strongylus* spp.) bots (*Gastrophilus* spp.), small strongyles, and pinworms (*Oxyuris equi*).¹

(3) **Limitations.** Withhold feed overnight or for 8 to 10 hours. Give water before and/or after treatment. Resume regular feeding 4 to 6 hours after treatment. Treatment of debilitated or anemic animals is contraindicated. Do not administer to animals that are or were recently affected with colic, diarrhea, or infected with a serious infectious disease. As with most anthelmintics, drastic cathartics or other gastrointestinal irritants should not be administered in conjunction with this drug. Animals in poor condition or heavily parasitized should be given one half the recommended dose and treated again in 2 or 3 weeks. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.¹

§ FR 52782, Aug. 8, 1980

§ 520.1802c Piperazine-carbon disulfide complex with phenothiazine suspension.

(a) **Specifications.** Each fluid ounce contains 5 grams of piperazine-carbon disulfide complex and 0.83 gram of phenothiazine.

(b) **Sponsor.** See 000009 in § 510.600(c) of this chapter.

(c) **Conditions of use: Horses and ponies.**—(1) **Amount.** One fluid ounce per 100 pounds of body weight.

(2) **Indications for use.** For removing ascarids (large roundworms, *Parascaris equorum*), bots (*Gastrophilus* spp.), small strongyles, and large strongyles (*Strongylus* spp.).

(3) **Limitations.** See § 520.1802a(c)(3).

§ FR 52782, Aug. 8, 1980

§ 520.1803 Piperazine citrate capsules.

(a) **Specifications.** Piperazine citrate capsules contain piperazine citrate equivalent to 140 milligrams of piperazine base in each capsule.

(b) **Sponsor.** See No. 000031 in § 510.600(c) of this chapter.

(c) **Conditions of use.** (1) It is used in dogs and cats for the removal of large roundworms (*Toxocara canis* and *Toxocara leonina*).

(2) The contents of 1 capsule should be mixed with the food of the animal for each 5 pounds, or fraction thereof of body weight, except dogs weighing over 25 pounds should be given the contents of 6 capsules. The drug should be mixed in ¼ of the regular feeding and when the animal has finished eating the dosed food, the remainder of the food may be given. Dogs and cats may be wormed at 6 to 8 weeks of age. The first treatment should be repeated 10 days later. Reinfection may occur. Repeat treatment if indicated.

(3) Severely debilitated animals should not be wormed except on the advice of a veterinarian.

§ 520.1804 Piperazine phosphate capsules.

(a) **Specifications.** Each capsule contains 120, 300, or 600 milligrams of piperazine phosphate monohydrate.

(b) **Sponsor.** See No. 050906 in § 510.600(c) of this chapter.

(c) **Conditions of use.**—(1) **Amount.** 60 milligrams of piperazine phosphate monohydrate per pound of body weight.¹

(2) **Indications for use.**—(i) **Dogs.** It is used for the removal of large roundworms (ascarids) *Toxocara canis* and *Toxascaris leonina*.¹

(ii) **Cats.** It is used for the removal of large roundworms (ascarids) *Toxocara mystax* and *Toxocaris leonina*.¹

(3) **Limitations.** Administer in animal's food or milk. For animals up to 1 year of age administer every 2 or 3 months; for animals over 1 year old, administer periodically as necessary. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.¹

[43 FR 6941, Feb. 17, 1978; 43 FR 9804, Mar. 10, 1978, as amended at 46 FR 20158, Apr. 3, 1981]

¹These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

§ 520.1805

§ 520.1805 Piperazine phosphate with thenium closylate tablets.

(a) *Specifications.* Each scored tablet contains the equivalent of 250 milligrams piperazine hexahydrate (as piperazine phosphate) and 125 milligrams thenium (as thenium closylate) or 500 milligrams piperazine hexahydrate (as piperazine phosphate) and 250 milligrams thenium (as thenium closylate).

(b) *Sponsor.* See No. 017220 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* Administer orally to dogs as follows:

NUMBER OF TABLETS AT EACH OF THE TWO DOSES

Animal weight (lb)	375 mg	750 mg
2 but less than 5	1/2	
5 but less than 10	1	1/2
10 or heavier	2	1

(2) *Indications for use.* For removal of immature (fourth stage larvae) and adult hookworms (*Ancylostoma caninum*, *A. braziliense*, and *Uncinaria stenocephala*) and ascarids (*Toxocara canis*) from weaned pups and adult dogs.

(3) *Limitations.* Do not use this product to treat dogs weighing less than 2 pounds, unweaned pups, or pups under 5 weeks of age. Maximum efficacy against hookworms necessitates two doses in 1 day of treatment. The interval between the doses should be not less than 4 hours or more than 24 hours. Administer the first dose in the morning before feeding. Do not permit dog to chew tablet. Feed the dog between doses. Do not feed milk or other fatty foods during treatment. Retreatment may be needed in 7 to 28 days as determined by laboratory fecal examinations or in animals kept in known contaminated quarters. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[43 FR 32747, July 28, 1978, as amended at 47 FR 55476, Dec. 10, 1982]

§ 520.1806 Piperazine monohydrochloride liquid.

(a) *Specifications.* The product contains 4.77 percent piperazine monohy-

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drochloride, equivalent to 3.35 percent piperazine base.

(b) *Sponsor.* See 017800 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Indications for use.* For dogs for the removal of roundworms (*Toxocara canis* and *Toxascaris leonina*).

(2) *Dosage.* Administer 20 to 30 milligrams of piperazine base per pound of body weight as a single dose.

(3) *Limitations.* Administer by mixing into the animal's ration to be consumed at one feeding. For animals in heavily contaminated areas, reworm at monthly intervals. Not for use in unweaned pups or animals less than three weeks of age. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

[47 FR 20758, May 14, 1982]

§ 520.1840 Poloxalene.

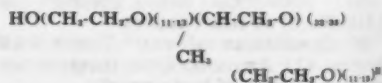
(a) *Chemical name.* Polyoxypropylene-polyoxyethylene glycol nonionic block polymer.

(b) *Specifications.* (1) Molecular weight range: 2,850 to 3,150.

(2) Hydroxyl number: 35.7 to 39.4.

(3) Cloud point (10 percent solution): 42° C.-46° C.

(4) Structural formula:



(c) *Sponsor.* (1) See No. 011519 in § 510.600(c) of this chapter for the sponsor of the usage provided by paragraph (d)(1) of this section.

(2) See No. 000007 in § 510.600(c) of this chapter for sponsor of usage provided by paragraph (d)(3) of this section.

(3) See No. 050112 in § 510.600(c) of this chapter for sponsor of usage provided by paragraph (d)(2) of this section.

(d) *Conditions of use.* (1) For treatment of legume (alfalfa, clover) bloat in cattle. Administer as a drench at the rate of 25 grams for animals up to 500 pounds and 50 grams for animals over 500 pounds of body weight.

(2) For control of legume (alfalfa, clover) bloat in cattle. Administer, in

molasses block containing 6.6 percent poloxalene, at the rate of 0.8 oz. of block (1.5 grams poloxalene) per 100 lbs. of body weight per day.

(3) For prevention of legume (alfalfa, clover) and wheat pasture bloat in cattle. A 53-percent poloxalene top dressing on individual rations of ground feed. Dosage is 1 gram of poloxalene per 100 pounds of body weight daily. If bloating conditions are severe, the dose is doubled. Treatment should be started 2 to 3 days before exposure to bloat-producing conditions. Repeat use of the drug if animals are exposed to bloat-producing conditions for more than 12 hours after the last treatment. Do not exceed the double dose in any 24-hour period.

[40 FR 13838, Mar. 27, 1975, as amended at 40 FR 39857, Aug. 29, 1975; 42 FR 41854, Aug. 19, 1977; 50 FR 5385, Feb. 8, 1985]

§ 520.1846 Polyoxyethylene (23) lauryl ether blocks.

(a) *Specifications.* Each molasses-based block contains 2.2 percent polyoxyethylene (23) lauryl ether.

(b) *Sponsor.* See No. 035624 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* 2 grams of polyoxyethylene (23) lauryl ether per 100 kilograms of body weight per day (1 pound of block per 500 kilogram (1,100 pound) animal per day).

(2) *Indications for use.* For reduction of the incidence of bloat (alfalfa and clover) in pastured cattle.

(3) *Limitations.* Administer free-choice to beef cattle and nonlactating dairy cattle only. Initially, provide one block per five head of cattle. Start treatment 10 to 14 days before exposure to bloat-producing pastures. Do not allow cattle access to other sources of salt while being fed this product. Do not feed this product to animals without adequate forage/roughage consumption.

[50 FR 48189, Nov. 22, 1985]

§ 520.1870 Praziquantel tablets.

(a) *Specifications.* Each dog tablet contains 34 milligrams (mgs) of praziquantel; each cat tablet contains 23 mgs of praziquantel.

(b) *Sponsor.* See No. 000859 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Dogs—(i) Indications for use.* For removal of canine cestodes *Dipylidium caninum*, *Taenia pisiformis*, and *Echinococcus granulosus*.

(ii) *Dosage.* Dogs 5 pounds and under, $\frac{1}{2}$ tablet (17 mgs); 6 to 10 pounds, 1 tablet (34 mgs); 11 to 15 pounds, $1\frac{1}{2}$ tablets (51 mgs); 16 to 30 pounds, 2 tablets (68 mgs); 31 to 45 pounds, 3 tablets (102 mgs); 46 to 60 pounds, 4 tablets (136 mgs); over 60 pounds, 5 tablets maximum (170 mgs).

(iii) *Limitations.* Administer directly by mouth or crumbled and in feed. Not intended for use in puppies less than 4 weeks of age. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(2) *Cats—(i) Indications for use.* For removal of feline cestodes *Dipylidium caninum* and *Taenia taeniaeformis*.

(ii) *Dosage.* Cats 4 pounds and under, $\frac{1}{2}$ tablet (11.5 mgs); 5 to 11 pounds, 1 tablet (23 mgs); over 11 pounds, $1\frac{1}{2}$ tablets (34.5 mgs).

(iii) *Limitations.* Administer directly by mouth or crumbled and in feed. Not intended for use in kittens less than 6 weeks of age. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[46 FR 60570, Dec. 11, 1981, as amended at 47 FR 26377, June 18, 1982]

§ 520.1900 Primidone tablets.

(a) *Specifications.* Each tablet contains 50 or 250 milligrams of primidone.

(b) *Sponsor.* See No. 054273 in § 510.600(c) of this chapter for use of 250 milligram tablets; see Nos. 000725 and 000856 in § 510.600(c) of this chapter for use of 50 and 250 milligram tablets.

(c) *Conditions of use in dogs—(1) Amount.* Twenty-five milligrams of primidone per pound of body weight (55 milligrams per kilogram of body weight) daily.¹

¹These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

§ 520.1920

(2) *Indications for use.* For the control of convulsions associated with idiopathic epilepsy, epileptiform convulsions, viral encephalitis, distemper, and hardpad disease that occurs as a clinically recognizable lesion in certain entities in dogs.¹

(3) *Limitations.* The tablets may be administered whole or crushed and mixed with the food. When convulsions are frequent, the dosage should be divided and administered at intervals. Reduction in dosage should be made gradually and never be abruptly discontinued. Do not use in feline species, as primidone appears to have a specific neurotoxicity in cats. Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

[42 FR 61594, Dec. 6, 1977, as amended at 43 FR 55386, Nov. 28, 1978; 46 FR 8467, Jan. 27, 1981; 46 FR 57477, Nov. 24, 1981; 53 FR 40727, Oct. 18, 1988]

§ 520.1920 Prochlorperazine, isopropamide sustained release capsules.

(a) *Specifications.* Prochlorperazine, isopropamide sustained release capsules contain either:

(1) 3.33 milligrams of prochlorperazine (as the dimaleate) and 1.67 milligrams of isopropamide (as the iodide), or

(2) 10 milligrams of prochlorperazine (as the dimaleate) and 5 milligrams of isopropamide (as the iodide).

(b) *Sponsor.* See No. 011519 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used for the treatment of dogs in which gastrointestinal disturbances are associated with emotional stress.

(2)(i) Capsules described in paragraph (a)(1) of this section are administered orally to dogs weighing from 4 to 15 pounds at the rate of 1 capsule twice daily. These capsules are administered orally to dogs weighing from 16 to 30 pounds at the rate of 1 or 2 capsules twice daily. For dogs weighing less than 4 pounds, administer orally an appropriate fraction of the contents of one of these capsules.

(ii) Capsules described in paragraph (a)(2) of this section are given to dogs weighing 30 pounds and over at the rate of 1 capsule twice daily.

¹See footnote 1 to § 520.1900.

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(3) For use only by or on the order of a licensed veterinarian.

§ 520.1921 Prochlorperazine, isopropamide, with neomycin sustained-release capsules.

(a) *Specifications.* Each capsule contains either:

(1) Capsule No. 1: 3.33 milligrams of prochlorperazine (as the dimaleate), 1.67 milligrams of isopropamide (as the iodide), and 25 milligrams of neomycin base (as the sulfate); or

(2) Capsule No. 3: 10 milligrams of prochlorperazine (as the dimaleate), 5 milligrams of isopropamide (as the iodide), and 75 milligrams of neomycin base (as the sulfate).

(b) *Sponsor.* See No. 011519 in § 510.600(c) of this chapter.

(c) *Conditions of use.*—(1) *Amount.* Administer capsules orally twice daily to dogs as follows:

Animal weight (pounds)	Number of capsules per dose	
	Capsule No. 1	Capsule No. 3
10 to 20	1	
20 to 30	2	
Over 30	3	1
Over 60		2

(2) *Indications for use.* For treatment of dogs in which infectious bacterial gastroenteritis is associated with emotional stress.

(3) *Limitations.* Do not continue medication longer than 5 days. Overdosage or prolonged administration may produce nephrotoxicity as manifested by albuminuria, presence of granular casts and depressed urinary output. If it is desirable to administer a vasoconstrictor, norepinephrine is the drug of choice. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[49 FR 14103, Apr. 10, 1984]

§ 520.1962 Promazine hydrochloride.

(a)(1) *Chemical name.* 10-[3-(Dimethylamino)propyl]phenothiazine monohydrochloride.

(2) *Specifications.* Conforms to N.F. XII.

(3) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(4) [Reserved]

(5) *Conditions of use.* (i) The drug is used for quieting excitable, unruly, or intractable horses. It is administered at a dosage level of 0.45 to 0.9 milligrams of promazine hydrochloride per pound of body weight mixed with an amount of feed that will be readily consumed.¹

(ii) Do not use in horses intended for food.¹

(iii) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

(b)(1) *Specifications.* Each tablet contains 25, 50, or 100 milligrams of promazine hydrochloride.

(2) *Sponsor.* No. 000008 in § 510.600(c) of this chapter.

(3) *Conditions of use—(i) Amount—Dogs and cats.* 1 to 3 milligrams orally per pound of body weight in intervals of 4 to 6 hours.¹

(ii) *Indications for use.* The drug is used for control of central nervous system excitation; allaying anxiety, nervousness and apprehension; calming agitated animals; and minimizing injury during shipment. As a preanesthetic agent, the drug potentiates effects of general anesthesia. It is indicated during physical and/or radiographic examination, radiographic diagnosis or therapy, and surgery. It reduces self-mutilation associated with sutures, bandages, eczema, pruritis, and otitis. Oral administration before vermifuge prevents emesis in cats.¹

(iii) *Limitations.* As with all phenothiazine-derived compounds, promazine should not be used in conjunction with organophosphates because their toxicity may be potentiated, nor with procaine hydrochloride for its activity may be increased. Prolonged depression or motor restlessness may occur in sensitive animals or on excessive dosing. For use only by or on the order of a licensed veterinarian.¹

¹These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

[40 FR 13838, Mar. 27, 1975, as amended at 43 FR 55386, Nov. 28, 1978]

§ 520.2002 Propiopromazine hydrochloride.

(a) *Chemical name.* 1-Propanone, 1-[10-[3-(dimethylamino) propyl] phenothiazine-2-yl]-, monohydrochloride.

(b) *Specifications.* The drug is administered in a chewable tablet containing 10 to 20 milligrams of propiopromazine hydrochloride.

(c) *Sponsor.* See No. 000033 in § 510.600(c) of this chapter.

(d) *Conditions of use.* (1) The drug is intended for oral administration to dogs as a tranquilizer. It is used as an aid in handling difficult, excited, and unruly dogs, and in controlling excessive kennel barking, car sickness, and severe dermatitis. It is also indicated for use in minor surgery and prior to routine examinations, laboratory procedures, and diagnostic procedures.

(2) It is administered at the rate of 0.5 to 2 milligrams of propiopromazine hydrochloride per pound of body weight once or twice daily depending upon the degree of tranquilization desired.

NOTE: Not for use with organophosphates and/or procaine hydrochloride, as phenothiazine may potentiate the toxicity of organophosphates and the activity of procaine hydrochloride. Overdosage may produce significant depression.

(3) For use only by or on the order of a licensed veterinarian.

[40 FR 13838, Mar. 27, 1975, as amended at 46 FR 60570, Dec. 11, 1981]

§ 520.2022 Protokylol hydrochloride tablets.

(a) *Specifications.* The drug is in tablet form with each tablet containing 0.5 or 2 milligrams of protokylol hydrochloride.

(b) *Sponsor.* See No. 000859 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is used in dogs and cats for the relief of bronchial spasm.¹

(2) It is administered three times a day (after feeding) at a level of 2 to 4 milligrams to dogs, 1 to 2 milligrams to

¹See footnote 1 to § 520.1962.

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cats, 0.5 to 1 milligram to puppies, and and 0.25 to 0.5 milligram to kittens.¹

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

§ 520.2041 Pyrantel pamoate chewable tablets.

(a) *Specifications.* Each tablet contains pyrantel pamoate equivalent to 22.7 or 113.5 milligrams pyrantel base.

(b) *Sponsor.* See No. 017800 in § 510.600(c) of this chapter.

(c) *Conditions of use.*—(1) *Amount.* Provides at least 2.27 milligrams pyrantel base per pound body weight for dogs weighing more than 5 pounds, and at least 4.54 milligrams of pyrantel base per pound body weight for dogs weighing 5 pounds or less.

(2) *Indications for use.* (i) In dogs and puppies. For removal of ascarids (*Toxocara canis*; *Toxascaris leonina*) and hookworms (*Ancylostoma caninum*; *Uncinaria stenocephala*).

(ii) In puppies and adult dogs and in lactating bitches after whelping. To prevent reinfection of *Toxocara canis*.

(3) *Limitations.* Administer to puppies at 2, 3, 4, 6, 8, and 10 weeks of age. Administer to lactating bitches 2 to 3 weeks after whelping. Retreatment of adult dogs may be necessary at monthly intervals as determined by laboratory fecal examinations. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

[52 FR 37937, Oct. 13, 1987]

§ 520.2042 Pyrantel pamoate tablets.

(a) *Specifications.* Each tablet contains pyrantel pamoate equivalent to 22.7, 45.4, or 113.5 milligrams of pyrantel base.

(b) *Sponsor.* See No. 017800 in § 510.600(c) of this chapter.

(c) *Conditions of use.* It is used for dogs as follows:

(1) *Amount.* For dogs weighing over 5 pounds, use at least 2.27 milligrams of pyrantel base per pound of body weight; for dogs weighing 5 pounds or less, use at least 4.54 milligrams of pyrantel base per pound of body weight.

(2) *Indications for use.* For removal and control of large roundworms (ascarids) (*Toxocara canis* and *Toxas-*

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caris leonina), and hookworms (*Ancylostoma caninum* and *Uncinaria stenocephala*).

(3) *Limitations.* Administer orally directly or in a small amount of food. To prevent reinfection of *T. canis* in puppies, lactating bitches after whelping, and adult dogs; treat puppies 2, 3, 4, 6, 8, and 10 weeks of age; treat lactating bitches 2 to 3 weeks after whelping; routinely treat adult dogs monthly. Do not withhold food prior to or after treatment. The presence of these parasites should be confirmed by laboratory fecal examination. A followup fecal examination should be conducted 2 to 4 weeks after first treatment regimen to determine the need for re-treatment. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

[43 FR 52700, Nov. 14, 1978, as amended at 49 FR 22073, May 25, 1984]

§ 520.2043 Pyrantel pamoate suspension.

(a)(1) *Specifications.* Pyrantel pamoate suspension contains pyrantel pamoate equivalent to 50 milligrams of pyrantel base per milliliter.

(2) *Sponsor.* See No. 000069 in § 510.600(c) of this chapter.

(3) *Conditions of use.* It is used in horses and ponies as follows:

(i) *Amount.* Equivalent of 3 milligrams pyrantel base per pound of body weight.

(ii) *Indications for use.* For the removal and control of infections from the following mature parasites: Large strongyles (*Strongylus vulgaris*, *Strongylus edentatus*, *Strongylus equinus*), small strongyles, pinworms (*Oxyuris*), and large roundworms (*Parascaris*).

(iii) *Limitations.* Administered as a single dose mixed with the usual grain ration, or by stomach tube, or by dose syringe. Not for use in horses and ponies to be slaughtered for food purposes. When the drug is for administration by stomach tube, it shall be labeled: "Federal law restricts this drug to use by or on the order of a licensed veterinarian." When the drug is not for administration by stomach tube, it shall be labeled: "Consult your veterinarian for assistance in the diagnosis, control, and treatment of parasitism."

(b)(1) *Specifications.* Pyrantel pamoate suspension contains pyrantel pamoate equivalent to 2.27 or 4.54 milligrams of pyrantel base per milliliter.

(2) *Sponsor.* See No. 000069 in § 510.600(c) of this chapter.

(3) *Conditions of use.* It is used in puppies and dogs as follows:

(i) *Amount.* Equivalent of 2.27 milligrams of pyrantel base per pound of body weight.

(ii) *Indications for use.* For the removal of large roundworms (*Toxocara canis* and *Toxascaris leonina*) and hookworms (*Ancylostoma caninum* and *Uncinaria stenocephala*).

(iii) *Limitations.* Administer in the animal's feed bowl as a single dose by itself or mixed in a small quantity of food. Additional treatment may be required and should be confirmed by fecal examination within 2 to 4 weeks. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

(4) *Conditions of use.* It is used in puppies and adult dogs and in lactating bitches after whelping as follows:

(i) *Amount.* Equivalent to 2.27 milligrams of pyrantel base per pound of body weight.

(ii) *Indications for use.* To prevent reinfections of *Toxocara canis*.

(iii) *Limitations.* Administer to puppies at 2, 3, 4, 6, 8, and 10 weeks of age. Administer to lactating bitches 2 to 3 weeks after whelping. Adult dogs kept in heavily contaminated quarters may be treated at monthly intervals. Consult your veterinarian for assistance in the diagnosis, treatment and control of parasitism.

(42 FR 28534, June 3, 1977, as amended at 44 FR 36381, June 22 1979; 45 FR 10760, Feb. 19, 1980; 47 FR 16776, Apr. 20, 1982; 51 FR 11440, Apr. 3, 1986)

§ 520.2044 Pyrantel pamoate paste.

(a) *Specifications.* Each milliliter of paste contains 180 milligrams of pyrantel base (as pyrantel pamoate).

(b) *Sponsor.* See 000069 in § 510.600(c) of this chapter.

(c) *Conditions of use.* It is used in horses and ponies as follows:

(1) *Amount.* Equivalent of 3 milligrams pyrantel base per pound of body weight.

(2) *Indications for use.* For removal and control of infections from the following mature parasites: large strongyles (*Strongylus vulgaris*, *S. edentatus*, *S. equinus*); small strongyles; pinworms (*Oxyuris equi*); and large roundworms (*Parascaris equorum*).

(3) *Limitations.* Administer as single dose by depositing paste on dorsum of the tongue using the dose syringe. Not for use in horses intended for food. It is recommended that severely debilitated animals not be treated with this preparation. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

[47 FR 47377, Oct. 26, 1982; 48 FR 3367, Jan. 25, 1983]

§ 520.2045 Pyrantel tartrate powder; pyrantel tartrate pellets.

(a) *Specifications.* (1) Pyrantel tartrate powder horse wormer contains 11.3 percent and swine wormer 10.6 percent pyrantel tartrate.

(2) Pyrantel tartrate pellets colt and horse wormer contains 1.25 percent pyrantel tartrate.

(b) *Sponsor.* (1) See No. 000069 in § 510.600(c) of this chapter for conditions of use provided for in paragraphs (d) (1) and (2) of this section.

(2) See No. 017800 in § 510.600(c) of this chapter, for conditions of use provided for in paragraph (d)(3) of this section.

(c) *Related tolerances.* See § 556.560 of this chapter.

(d) *Conditions of use.* It is used in:

(1) Horses and ponies:

(i) For the removal and control of infections from the following mature parasites: Large strongyles (*Strongylus vulgaris*, *Strongylus edentatus*, *Strongylus equinus*), small strongyles (*Trichonema* spp., *Triodontophorus*), pinworms (*Oxyuris*), and large roundworms (*Parascaris*).

(ii) It is administered as a single dose at 0.57 gram of pyrantel tartrate per 100 pounds of body weight mixed with the usual grain ration.

(iii) It is recommended that severely debilitated animals not be treated with this drug. Do not administer by stomach tube or dose syringe. The drug should be used immediately after the package is opened.

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(iv) Warning: Not for use in horses and ponies to be slaughtered for food purposes.

(2) Swine:

(i) For the removal and control of large roundworms (*Ascaris suum*) and nodular worm (*Oesophagostomum*) infections.

(ii) It is added to feed at 0.4 gram pyrantel tartrate per pound of nonpelleted ration. The ration is administered as a single treatment as the sole ration at the rate of 1 pound per 40 pounds of animal weight for animals up to 200 pounds. Animals 200 pounds and over are administered 5 pounds of ration per animal.

(iii) Fast pigs over night for optimum results. Water should be made available to animals during fasting and treatment periods. Consult veterinarian before using in severely debilitated animals. The drug should be used immediately after the package is opened.

(iv) Warning: Do not treat within 24 hours of slaughter.

(3) Horses and colts:

(i) For the removal and control of infections from the following mature parasites: Large strongyles (*Strongylus vulgaris*, *Strongylus edentatus*, *Strongylus equinus*), small strongyles (*Triodontophorus* spp., *Triodontophorus*), pinworms (*Oxyuris*), and large roundworms (*Parascaris*).

(ii) It is administered as a single dose at 12.5 milligrams of pyrantel tartrate per 2.2 pounds of body weight mixed with the usual grain ration.

(iii) It is recommended that severely debilitated animals not be treated with this drug.

(iv) Warning: Do not use in horses or colts intended for food.

§ 520.2080 Ronnel oral dosage forms.

[48 FR 15243, Apr. 8, 1983]

§ 520.2080a Ronnel blocks.

(a) *Specifications.* Each pound of block contains 25 grams of ronnel (5.5 percent).

(b) *Sponsor.* See 021930 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See 40 CFR 180.177.

(d) *Conditions of use—(1) Amount.* 0.25 pound of block (6.24 grams of ronnel) per 100 pounds of body weight

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per head per month for not less than 75 days.

(2) *Indications for use.* Control of grubs and hornflies.

(3) *Limitations.* Administer free choice to beef cattle and nonlactating dairy animals. Provide 1 block per 15 head of cattle. Use as sole source of ronnel. Do not allow cattle access to salt or other mineral while being fed this product. Withdraw from dairy animals 10 days before calving. If animals freshen during medication, or if medication has not been withdrawn 10 days before freshening, milk must not be used for food for 10 days after the last treatment. Withdraw 10 days before slaughter. Labeling shall also include a warning that ronnel is a cholinesterase inhibitor. Do not use this product simultaneously or within a few days before or after exposure to cholinesterase inhibiting drugs, pesticides, or chemicals.

[48 FR 15243, Apr. 8, 1983]

§ 520.2080b Ronnel tablets.

(a) *Specifications.* Each tablet contains 250 milligrams, 500 milligrams, or 1 gram of ronnel.

(b) *Sponsor.* See No. 011716 in § 510.600(c) of this chapter.

(c) *Generic status.* These conditions of use were reviewed and found effective by FDA before October 10, 1962. New animal drug applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(d) *Conditions of use—(1) Indications for use.* Dogs: Treatment of demodectic mange, tick, flea, and lice infections. Cats: Treatment of flea infestations.

(2) *Dosage.* (i) Demodectic mange in dogs: 25 milligrams per pound of body weight daily, preferably in divided doses; in very severe infections, 35 milligrams per pound of body weight daily; continue treatment 3 weeks after all mites in skin scrapings are dead.

(ii) Ticks in dogs: 50 milligrams per pound of body weight daily in single or divided doses; when improvement noted, reduce to maintenance level of

12.5 milligrams per pound of body weight daily.

(iii) Fleas and lice in dogs, or fleas in cats: 25 milligrams per pound of body weight every other day in single or divided doses; with continued control, decrease to 12.5 milligrams per pound of body weight every other day.

(3) *Limitations.* Oral treatment of hemodectic mange or ticks in dogs may be combined with application of topical ronnel solutions. Ronnel is a cholinesterase inhibitor. Do not use this product on animals simultaneously or within a few days before or after treatment with or exposure to cholinesterase inhibiting drugs, pesticides, or chemicals. Atropine is an antidote. Treat symptomatically. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

§ 520.2088, Apr. 8, 1983]

§ 520.2087 Roxarsone soluble powder.

(a) *Specifications.* Each ounce (avirdupois) of soluble powder contains 7 grams of roxarsone (monosodium nitro-4-hydroxyphenylarsonate).

(b) *Sponsor.* See No. 017210 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See § 556.60 of this chapter.

(d) *NAS/NRC status.* These conditions of use are NAS/NRC reviewed and found effective. NADA's for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(e) *Conditions of use—(1) Growing chickens and growing turkeys—(i) Amount.* 0.002 percent, roxarsone in drinking water (one packet per each 50 gallons of drinking water).

(ii) *Indications for use.* For increased rate of weight gain, improved feed efficiency, and improved pigmentation.

(iii) *Limitations.* Administer continuously throughout growing period. Withdraw 5 days before slaughter. Use as sole source of organic arsenic.

(2) *Swine—(i) Amount.* 0.01 percent roxarsone in drinking water (one packet per each 50 gallons of drinking water); or 30 milliliters of a 1.55 percent roxarsone solution (one packet per 3 pints of water) per 50 pounds of body weight as a drench.

(ii) *Indications for use.* As an aid in the treatment of swine dysentery (hemorrhagic enteritis or bloody scours).

(iii) *Limitations.* Administer drinking water continuously for not more than 6 days. Administer drench once daily for 1 or 2 days. If no improvement is observed, consult a veterinarian. Treatment may be repeated after 5 days. Withdraw 5 days before slaughter. Use as sole source of organic arsenic.

[46 FR 41039, Aug. 14, 1981]

§ 520.2088 Roxarsone tablets.

(a)(1) *Specifications.* Each tablet contains 36 milligrams of roxarsone (3-nitro-4-hydroxyphenylarsonic acid).

(2) *Sponsor.* See No. 017210 in § 510.600(c) of this chapter.

(3) *Related tolerances.* See § 556.60 of this chapter.

(4) *NAS/NRC status.* The weight gain, feed efficiency, and pigmentation claims are NAS/NRC reviewed and found effective. NADA's for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(5) *Conditions of use—(i) Growing chickens and growing turkeys—(a) Amount.* Dissolve 2 tablets in each gallon of drinking water (0.002 percent roxarsone).

(b) *Indications for use.* For increased rate of weight gain, improved feed efficiency, and improved pigmentation.

(c) *Limitations.* Administer continuously throughout growing period. Withdraw 5 days before slaughter. Use as sole source of organic arsenic.

(ii) *Growing chickens—(a) Amount.* Dissolve 8 tablets in each gallon of drinking water (0.008 percent roxarsone).

(b) *Indications for use.* As an aid in the prevention of coccidiosis due to *Eimeria tenella*.

(c) *Limitations.* Administer for not more than 10 consecutive days. Treatment may be repeated after 5 days off medication. Withdraw 5 days before slaughter. Use as sole source of organic arsenic.

(b)(1) *Specifications.* Each tablet contains 400 milligrams of roxarsone (3-nitro-4-hydroxyphenylarsonic acid).

(2) *Sponsor.* See No. 017210 in § 510.600(c) of this chapter.

(3) *Related tolerances.* See § 556.60 of this chapter.

(4) *NAS/NRC status.* These conditions are NAS/NRC reviewed and found effective. NADA's for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(5) *Conditions of use—(i) Swine—(a) Amount.* 1 tablet (400 milligrams) per gallon of drinking water for no more than 6 days, or 1 tablet (400 milligrams) per 2 fluid ounces of warm water per 50 pounds of body weight as a drench once daily for 1 to 2 days.

(b) *Indications for use.* As an aid in the treatment of swine dysentery (hemorrhagic enteritis or bloody scours).

(c) *Limitations.* Treatment may be repeated after 5 days off medication. If no improvement is observed, consult a veterinarian. Treated animals must consume enough medicated water to provide a therapeutic dose. Withdraw 5 days before slaughter. Use as sole source of organic arsenic.

(ii) [Reserved]

[46 FR 41040, Aug. 14, 1981, as amended at 46 FR 42448, Aug. 21, 1981; 47 FR 15238, Apr. 9, 1982]

§ 520.2100 Selenium, vitamin E capsules.

(a) *Specifications.* The capsules contain 2.19 milligrams of sodium selenite (equivalent to 1 milligram of selenium) and 56.2 milligrams of vitamin E (68 I.U.) (as d-alpha tocopheryl acid succinate) or 0.548 milligram of sodium selenite (equivalent to .25 milligram of selenium and 14 milligrams of vitamin E (17 I.U.) (as d-alpha tocopheryl acid succinate.)

(b) *Sponsor.* See No. 000061 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is intended for use as an aid in alleviating and controlling inflammation, pain, and lameness associated with certain arthropathies in dogs.

(2) The capsules are administered orally with the larger capsules administered at a dosage level of 1 capsule

per 20 pounds of body weight to a maximum of 5 capsules with the dosage repeated at 3 day intervals until a satisfactory therapeutic response is observed. A maintenance dosage is then administered consisting of 1 capsule per 40 pounds of body weight, with a minimum of 1 capsule per 40 pounds of body weight, with a minimum of 1 capsule, given every 3 days, or 7 days, or longer, as required to maintain improvement or an asymptomatic condition. For dogs under 20 pounds of body weight, the small capsules are administered orally at a dosage level of 1 per 5 pounds of body weight with a minimum of 1 capsule which dosage is repeated at 3 day intervals until a satisfactory response is observed then a maintenance regimen is initiated with 1 capsule per 10 pounds of body weight, minimum of 1 capsule, every 3 days, or 7 days, or longer as required to maintain continued improvement or an asymptomatic condition.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13838, Mar. 27, 1975, as amended at 52 FR 7832, Mar. 13, 1987; 52 FR 9756, Mar. 26, 1987]

§ 520.2122 Spectinomycin dihydrochloride oral solution.

(a) *Specifications.* The spectinomycin dihydrochloride pentahydrate used in manufacturing the drug is the antibiotic substance produced by growth of *Streptomyces flavopersicus* (var. Abbott) or the same antibiotic substance produced by any other means. The drug is packaged as an aqueous solution containing 50 milligrams of spectinomycin activity per milliliter.

(b) *Sponsors.* (1) See No. 050604 in § 510.600(c) of this chapter.

(2) See No. 000033 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is used for the treatment and control of infectious bacterial enteritis (white scours) associated with *E. coli* in pigs under 4 weeks of age.

(2) It is administered orally at the rate of 50 milligrams per 10 pounds body weight twice daily for 3 to 5 days.

(3) Do not administer to pigs over 15 pounds body weight or over 4 weeks of age. Do not administer within 21 days of slaughter.

[40 FR 13838, Mar. 27, 1975, as amended at 45 FR 56798, Aug. 26, 1980; 46 FR 60570, Dec. 11, 1981]

§ 520.2123 Spectinomycin dihydrochloride pentahydrate oral dosage forms.

§ 520.2123a Spectinomycin dihydrochloride pentahydrate tablets.

(a) *Specifications.* The spectinomycin dihydrochloride pentahydrate used in manufacturing the drug is the antibiotic substance produced by growth of *Streptomyces flavopersicus* (var. Abbott) or the same antibiotic substance produced by any other means.

(b) *Sponsor.* See No. 050604 in § 510.600(c) of this chapter.

(c) *Special considerations.* The quantities of spectinomycin cited in this section refer to the equivalent weight of base activity for the drug.

(d) *Conditions of use.* (1) The tablets are administered orally to dogs in the treatment of infectious diarrhea and gastroenteritis caused by organisms susceptible to spectinomycin.

(2) The drug is administered orally to provide 10 milligrams per pound of body weight twice daily. The tablets may be placed in the animal's mouth or crushed and administered in milk or in the feed. Dosage may be continued for 4 consecutive days. Should no improvement be observed, discontinue drug and redetermine diagnosis.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13838, Mar. 27, 1975, as amended at 47 FR 14149, Apr. 2, 1982]

§ 520.2123b Spectinomycin dihydrochloride pentahydrate soluble powder.

(a) *Specifications.* The spectinomycin dihydrochloride pentahydrate used in manufacturing the drug is the antibiotic substance produced by growth of *Streptomyces flavopersicus* (var. Abbott) or the same antibiotic substance produced by any other means.

(b) *Sponsor.* See No. 050604 in § 510.600(c) of this chapter.

(c) *Special considerations.* The quantities of spectinomycin cited in

this section refer to the equivalent weight of base activity for the drug.

(d) *Related tolerances.* See § 556.600 of this chapter.

(e) *Conditions of use.* (1) It is administered in the drinking water of growing chickens at 2 grams of spectinomycin per gallon of water as the only source of drinking water for the first 3 days of life and for 1 day following each vaccination. It is administered as an aid in the prevention or control of losses due to CRD associated with *M. gallisepticum* (PPLO). Do not administer to laying chickens. Do not administer within 5 days of slaughter.

(2) It is administered in the drinking water of floor-raised broiler chickens at 0.5 gram of spectinomycin per gallon of water as the only source of drinking water for the first 3 days of life and for 1 day following each vaccination. It is administered for increased rate of weight gain and improved feed efficiency. Do not administer to laying chickens. Do not administer within 5 days of slaughter.

(3) It is administered in drinking water of broiler chickens at 1 gram of spectinomycin per gallon of water as the only source of drinking water for the first 3 to 5 days of life as an aid in controlling infectious synovitis due to *Mycoplasma synoviae*. Do not administer to laying chickens. Do not administer within 5 days of slaughter.

[40 FR 13838, Mar. 27, 1975, as amended at 45 FR 56798, Aug. 26, 1980]

§ 520.2150 Stanazolol oral dosage forms.

[50 FR 38114, Sept. 20, 1985]

§ 520.2150a Stanazolol tablets.

(a) *Specifications.* Each tablet contains 2 milligrams of stanozolol.

(b) *Sponsor.* No. 000934 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) Used as an anabolic steroid treatment in dogs and cats.

(2) Administered orally to cats and small breeds of dogs, $\frac{1}{2}$ to 1 tablet twice daily for several weeks; to large breeds of dogs, 1 to 2 tablets twice daily for several weeks. The tablets may be crushed and administered in feed.

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(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 46101, Oct. 8, 1975, as amended at 42 FR 36995, July 19, 1977. Redesignated at 50 FR 38114, Sept. 20, 1985]

§ 520.2150b Stanozolol chewable tablets.

(a) *Specifications.* Each chewable tablet contains 2 milligrams of stanozolol.

(b) *Sponsor.* No. 000934 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) Used as an anabolic steroid treatment in dogs.

(2) Administered orally to small breeds of dogs, $\frac{1}{4}$ to 1 tablet twice daily for several weeks; to large breeds of dogs, 1 to 2 tablets twice daily for several weeks.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[50 FR 38114, Sept. 20, 1985]

§ 520.2155 Starch, pregelatinized.

(a) *Specifications.* Pregelatinized starch conforms to National Formulary XV requirements.

(b) *Sponsor.* See No. 052292 in § 510.600(c) of this chapter.

(c) *Conditions of use.* It is used in nonmedicated liquid feed or water of newborn calves as follows:

(1) *Amount.* 30 grams, twice daily.

(2) *Indications for use.* For the symptomatic treatment (i.e., increasing fecal consistency) of nonspecific diarrhea.

(3) *Limitations.* If septicemia or respiratory disease are suspected or scours persist for more than 2 days, consult your veterinarian.

[48 FR 56205, Dec. 20, 1983]

§ 520.2160 Styrylpyridinium, diethylcarbamazine oral dosage forms.

[46 FR 38505, July 28, 1981]

§ 520.2160a Styrylpyridinium, diethylcarbamazine tablets.

(a) *Specifications.* Each tablet contains 50 milligrams of styrylpyridinium chloride and 60 milligrams of diethylcarbamazine citrate, or 125 milligrams of styrylpyridinium chloride

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and 150 milligrams of diethylcarbamazine citrate.

(b) *Sponsor.* See No. 000859 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) For oral administration to dogs as an aid in the control of large roundworms (*Toxocara canis*) and hookworms (*Ancylostoma caninum*) and in the prevention of heartworm disease (*Dirofilaria immitis*).

(2) Administer orally, intact or pulverized and mixed in feed, at one tablet (50- and 50-milligram dosage) per 20 pounds of body weight per day, or one tablet (125- and 150-milligram dosage) per 50 pounds of body weight per day.

(3) Dogs with established heartworm infections should not be treated until they have been converted to a negative status. Administration to heartworm infected dogs may cause adverse reactions due to pulmonary occlusion.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[46 FR 38505, July 28, 1981, as amended at 47 FR 14150, Apr. 2, 1982]

§ 520.2160b Styrylpyridinium chloride diethylcarbamazine (as base).

(a) *Specifications.* Each milliliter of the drug contains 50 milligrams of styrylpyridinium chloride and 30 milligrams of diethylcarbamazine (as base).

(b) *Sponsor.* See No. 000859 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) For oral administration to dogs for the control of large roundworms (*Toxocara canis*) and hookworms (*Ancylostoma caninum*) and as an aid in the prevention of heartworm disease (*Dirofilaria immitis*).

(2) Administer the drug in food at 1 milliliter per 20 pounds of body weight daily during periods of exposure to roundworm, hookworm, and/or heartworm infections.

(3) Periodic examinations for large roundworms and heartworms should be made to assure that medication is given properly. Dogs with established heartworm infections should not be treated until they have been converted to a negative status. Administration to heartworm infected dogs may cause

adverse reactions due to pulmonary occlusion.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[46 FR 38505, July 28, 1981, as amended at 47 FR 14150, Apr. 2, 1982]

§ 520.2160c Styrylpyridinium, diethylcarbamazine edible tablets.

(a) *Specifications.* Each edible tablet contains the equivalent of 50 milligrams of styrylpyridinium chloride and 60 milligrams of diethylcarbamazine citrate, or 125 milligrams of styrylpyridinium chloride and 150 milligrams of diethylcarbamazine citrate, adsorbed on an inert resin.

(b) *Sponsor.* See No. 000859 in § 510.900(c) of this chapter.

(c) *Conditions of use.* (1) For oral administration to dogs as an aid in the control of large roundworms (*Toxocara canis*) and hookworms (*Ancylostoma caninum*) and in the prevention of heartworm disease (*Dirofilaria immitis*).

(2) Administer orally, intact or pulverized and mixed in feed, at one tablet (50- and 60-milligram dosage) per 20 pounds of body weight per day, or one tablet (125- and 150-milligram dosage) per 50 pounds of body weight per day.

(3) Dogs with established heartworm infections should not be treated until they have been converted to a negative status. Administration to heartworm infected dogs may cause adverse reactions due to pulmonary occlusion.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[46 FR 38506, July 28, 1981, as amended at 47 FR 14150, Apr. 2, 1982]

§ 520.2160d Styrylpyridinium, diethylcarbamazine film-coated tablets.

(a) *Specifications.* Each film-coated tablet contains the equivalent of 50 milligrams of styrylpyridinium chloride and 60 milligrams of diethylcarbamazine citrate, or 87.5 milligrams of styrylpyridinium chloride and 105 milligrams of diethylcarbamazine citrate, or 125 milligrams of styrylpyridinium chloride and 150 milligrams of diethylcarbamazine citrate, or 162.5 milli-

grams of styrylpyridinium chloride and 195 milligrams of diethylcarbamazine citrate.

(b) *Sponsor.* See No. 000859 in § 510.600(c) of this chapter.

(c) *Conditions of use.*—(1) *Amount.* The equivalent of 2.5 milligrams of styrylpyridinium chloride and 3 milligrams of diethylcarbamazine citrate per pound of body weight per day.

(2) *Indications for use.* Administer to dogs as an aid in the control of large roundworms (*Toxocara canis*) and hookworms (*Ancylostoma caninum*) and in the prevention of heartworm disease (*Dirofilaria immitis*).

(3) *Limitations.* Dogs with established heartworm infections should not be treated until they have been converted to a negative status. Administration to heartworm infected dogs may cause adverse reactions due to pulmonary occlusion.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[46 FR 46316, Sept. 18, 1981, as amended at 47 FR 14150, Apr. 2, 1982]

§ 520.2170 Sulfabromomethazine sodium boluses.

(a) *Specifications.* Each bolus contains 15 grams of sulfabromomethazine sodium.

(b) *Related tolerance.* See § 556.620 of this chapter.

(c) *Sponsor.* See No. 000006 in § 510.600(c) of this chapter.

(d) *NAS/NRC status.* These conditions of use are NAS/NRC reviewed and found effective. NADA's for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(e) *Conditions of use: Cattle.*—(1) *Amount.* 90 milligrams per pound body weight.

(2) *Indications for use.* Treatment of necrotic pododermatitis (foot rot) and calf diphtheria caused by *Fusobacterium necrophorum*; colibacillosis (scours) caused by *Escherichia coli*; bacterial pneumonia and bovine respiratory disease complex (shipping fever complex) associated with *Pasteurella* spp.; acute metritis and acute mastitis caused by *Streptococcus* spp.

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(3) *Limitations.* Administer orally; repeat in 48 hours if necessary; milk taken from animals within 96 hours (8 milkings) of latest treatment must not be used for food; do not administer within 18 days of slaughter; discontinue use if hematuria, crystalluria or severe depression are noticed; if signs persist after 2 or 3 days consult a veterinarian.

[47 FR 30243, July 13, 1982]

§ 520.2184 Sodium sulfachloropyrazine monohydrate.

(a) *Chemical name.* 2-Sulfamido-6-chloroxyrazine, sodium.

(b) *Sponsor.* See Nos. 010042 and 017210 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See § 556.625 of this chapter.

(d) *Conditions of use.* It is used in the drinking water of broilers, breeder flocks, and replacement chickens as follows:

(1) *Amount.* 0.03 percent.

(2) *Indications for use.* Treatment of coccidiosis.

(3) *Limitations.* Administer in drinking water for 3 days as sole source of drinking water and sulfonamide medication; withdraw 4 days prior to slaughter; not to be administered to chickens producing eggs for human consumption.

[40 FR 13838, Mar. 27, 1975, as amended at 50 FR 41489, Oct. 11, 1985; 53 FR 12188, Mar. 24, 1988]

§ 520.2200 Sulfachlorpyridazine oral dosage forms.

§ 520.2200a Sulfachlorpyridazine bolus.

(a) *Chemical name.* N'-6-(Chloro-3-pyridazinyl) sulfanilamide.

(b) *Specifications.* Melting point range: 190° C to 191° C.

(c) *Sponsor.* See No. 053501 in § 510.600(c) of this chapter.

(d) *Related tolerances.* See § 556.630 of this chapter.

(e) *Conditions of use.* It is used in calves as follows:

(1) *Amount.* 30 to 45 milligrams per pound body weight per day.

(2) *Indications for use.* Treatment of diarrhea caused or complicated by *E. coli* (colibacillosis).

(3) *Limitations.* Administer in a bolus containing 2 grams of sulfachlor-

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pyridazine for 1 to 5 days in divided doses twice daily; treated calves must not be slaughtered for food during treatment or for 7 days after the last treatment.

[40 FR 13838, Mar. 27, 1975, as amended at 50 FR 41489, Oct. 11, 1985]

§ 520.2200b Sulfachlorpyridazine medicated milk and drinking water.

(a) *Chemical name.* N'-6-Chloro-3-pyridazinyl sulfanilamide.

(b) *Specifications.* Melting point range: 190° C to 191° C.

(c) *Sponsor.* See No. 053501 in § 510.600(c) of this chapter.

(d) *Related tolerances.* See § 556.630 of this chapter.

(e) *Conditions of use.* It is used as follows:

(1) *Calves*—(i) *Amount.* 30 to 45 milligrams per pound body weight per day.

(ii) *Indications for use.* Treatment of diarrhea caused or complicated by *E. coli* (colibacillosis).

(iii) *Limitations.* Administer as the sodium salt of sulfachlorpyridazine in milk or milk-replacer formulations for 1 to 5 days in divided doses twice daily; treated calves must not be slaughtered for food during treatment or for 7 days after the last treatment.

(2) *Swine*—(i) *Amount.* 20 to 35 milligrams per pound body weight per day.

(a) *Indications for use.* Treatment of diarrhea caused or complicated by *E. coli* (colibacillosis).

(b) *Limitations.* Administer as the sodium salt of sulfachlorpyridazine in drinking water for 1 to 5 days; for individual treatment, administer orally in divided doses twice daily; treated swine must not be slaughtered for food during treatment or for 4 days after the last treatment.

(ii) *Amount.* 20 to 35 milligrams per pound body weight per day.

(a) *Indications for use.* Treatment of diarrhea caused or complicated by *E. coli* (colibacillosis).

(b) *Limitations.* Administer individually in an oral suspension containing 50 milligrams of sulfachlorpyridazine per milliliter in divided doses twice daily for 1 to 5 days; treated swine must not be slaughtered for food

during treatment or for 4 days after the last treatment.

(40 FR 13838, Mar. 27, 1975, as amended at 50 FR 41489, Oct. 11, 1985)

§ 520.2220c Sulfachlorpyridazine tablets.

(a) *Specifications.* Sulfachlorpyridazine tablets contain 250 milligrams of sulfachlorpyridazine per tablet.

(b) *Sponsor.* See No. 053501 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used in dogs as a broad spectrum antibacterial agent to aid in the treatment of infectious tracheobronchitis and infections caused by *E. coli*. It can also be used in the treatment of infections caused by other gram-positive and gram-negative organisms that are susceptible to sulfonamide therapy.

(2) It is administered orally at a dosage level of 500 milligrams per 10 to 15 pounds of body weight daily, in two or three divided doses.

(3) The administration of the drug should be discontinued if a response is not noted within 7 to 10 days.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(43 FR 36622, Aug. 18, 1978, as amended at 50 FR 41489, Oct. 11, 1985)

§ 520.2220 Sulfadimethoxine oral dosage forms.

§ 520.2220a Sulfadimethoxine drinking water and drench.

(a) *Chemical name.* N-(2,6-Dimethoxy-4-pyrimidinyl) sulfanilamide.

(b) *Sponsors.* Firms identified by numbers in § 510.600(c) of this chapter have been granted approvals for specific conditions of use as indicated in paragraph (e) of this section as follows: (1) To 000004: Approval for use as in paragraphs (e) (1), (2) and (3).

(c) *Special considerations.* Chickens and turkeys that have survived fowl cholera outbreaks should not be kept or replacements or breeders.

(d) *Related tolerances.* See § 556.640 of this chapter.

(e) *Conditions of use.* It is used as follows:

(1) *Broiler and replacement chickens only.* (i) *Amount.* 1.875 (0.05 percent) grams per gallon.

(ii) *Indications for use.* Treatment of disease outbreaks of coccidiosis, fowl cholera, and infectious coryza.

(iii) *Limitations.* Administer for 8 consecutive days; do not administer to chickens over 16 weeks of age; as sole source of drinking water and sulfonamide medication; as sulfadimethoxine solution or sulfadimethoxine soluble sodium salt; withdraw 5 days before slaughter.

(2) *Meal-producing turkeys only—(i) Amount.* 0.938 (0.025 percent) grams per gallon.

(ii) *Indications for use.* Treatment of disease outbreaks of coccidiosis and fowl cholera.

(iii) *Limitations.* Administer for 6 consecutive days; do not administer to turkeys over 24 weeks of age; as sole source of drinking water and sulfonamide medication; as sulfadimethoxine solution or sulfadimethoxine soluble sodium salt; withdraw 5 days before slaughter.

(3) *Dairy calves, dairy heifers, and beef cattle only—(i) Amount.* 1.18 to 2.36 (0.031 to 0.062 percent) grams per gallon.

(ii) *Indications for use.* Treatment of shipping fever complex, bacterial pneumonia, calf diphtheria, and foot rot.

(iii) Administer 2.5 grams per 100 pounds of body weight for first day, then 1.25 grams per 100 pounds of body weight per day for the next 4 consecutive days; in drinking water or drench; available as a sulfadimethoxine soluble powder or a 12.5 percent sulfadimethoxine sodium solution (3.75 grams sulfadimethoxine per fluid ounce); if no improvement within 2 to 3 days, reevaluate diagnosis; do not treat beyond 5 days; withdraw 7 days before slaughter.

§ 520.2220b Sulfadimethoxine tablets and boluses.

(a) *Chemical name.* N-(2,6-Dimethoxy-4-pyrimidinyl) sulfanilamide.

(b) *Sponsors.* Firms identified by numbers in § 510.600(c) of this chapter have been granted approvals for specific conditions of use as indicated in paragraph (e) of this section as follows:

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(1) To 000004: approval for use as in paragraphs (e) (1) and (3) of this section.

(2) [Reserved]

(3) To 011716: approval for use as in paragraph (e)(2)(ii) of this section.

(c) [Reserved]

(d) *Related tolerances.* See § 556.640 of this chapter.

(e) It is used as follows:

(1) *Cattle*—(i) *Amount.* 1.25 to 2.5 grams per 100 pounds body weight.

(ii) *Indications for use.* Treatment of foot rot, bacterial pneumonia, shipping fever, and calf diphtheria.

(iii) *Limitations.* Administer 2.5 grams per 100 pounds body weight for 1 day followed by 1.25 grams per 100 pounds body weight per day; treat from 4 to 5 days; do not administer within 7 days of slaughter; milk that has been taken from animals during treatment and 60 hours (5 milkings) after the latest treatment must not be used for food.

(2) *Dogs and cats*—(i) [Reserved]

(ii) *Amount.* 12.5 to 25 milligrams per pound body weight.

(a) *Indications for use.* Treatment of sulfadimethoxine-susceptible bacterial infections.

(b) *Limitations.* Administer 25 milligrams per pound body weight for first day followed by 12.5 milligrams per pound body weight per day until the animal is free of symptoms for 48 hours, for use only by or on the order of a licensed veterinarian.

(3) *Beef cattle and nonlactating dairy cattle*—(i) *Amount.* 12.5-gram-sustained-release bolus.

(ii) *Indications for use.* Treatment of shipping fever complex and bacterial pneumonia associated with organisms such as *Pasteurella* spp. sensitive to sulfadimethoxine; calf diphtheria and foot rot associated with *Sphaerophorus necrophorus* sensitive to sulfadimethoxine.

(iii) *Limitations.* Administer one bolus for the nearest 200 pounds of body weight, i.e., 62.5 milligrams per pound of body weight. Do not repeat treatment for 7 days. Do not use in lactating dairy cattle. Do not administer within 12 days of slaughter. During treatment make certain that animals maintain adequate water intake. Fed-

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eral law restricts this drug to use by or on the order of a licensed veterinarian.

(Sec. 512(e), 82 Stat. 345-347 (21 U.S.C. 360b(e)))

[40 FR 13838, Mar. 27, 1975, as amended at 40 FR 43488, Sept. 22, 1975; 49 FR 36830, Sept. 20, 1984]

§ 520.2220c Sulfadimethoxine oral suspension.

(a) *Chemical name.* *N*-(2,6-Dimethoxy-4-pyrimidinyl) sulfanilamide.

(b) *Specifications.* Each milliliter of the drug contains 50 milligrams of sulfadimethoxine.

(c) *Sponsor.* See Nos. 000004 and 011716 in § 510.600(c) of this chapter.

(1) It is intended for use in the treatment of sulfonamide susceptible bacterial infections in dogs and cats and enteritis associated with coccidiosis in dogs.

(2) On the first day of treatment administer an oral dose of 25 milligrams per pound of body weight, then follow with a daily dosage of 12.5 milligrams per pound of body weight. Length of treatment will depend upon clinical response. Continue treatment until patient is asymptomatic for 48 hours. Maintain adequate water intake during the treatment period.

(3) For use only by or on the order of a licensed veterinarian.

§ 520.2240 Sulfaethoxypyridazine.

§ 520.2240a Sulfaethoxypyridazine drinking water.

(a) *Chemical name.* *N*-(6-Ethoxy-3-pyridazinyl) sulfanilamide.

(b) *Specifications.* Melting point range of 180° C. to 186° C.

(c) *Sponsor.* See No. 010042 in § 510.600(c) of this chapter.

(d) *Related tolerances.* See § 556.650 of this chapter.

(e) *Conditions of use.* It is used as follows:

(1) *Swine*—(i) *Amount.* 1.9 to 3.8 grams per gallon (0.05 percent to 0.1 percent).

(ii) *Indications for use.* Treatment of bacterial scours pneumonia enteritis, bronchitis, septicemia accompanying *Salmonella choleraesuis* infection.

(iii) *Limitations.* Administer 3.8 grams per gallon for first day followed

by 1.9 grams per gallon for not less than 3 days nor more than 9 days as sodium sulfaethoxy-pyridazine; do not treat within 10 days of slaughter; as sole source of sulfonamide; for use by or on the order of a licensed veterinarian.

(2) *Cattle*—(i) *Amount*. 2.5 grams per gallon (0.066 percent).

(ii) *Indications for use*. Treatment of respiratory infections (pneumonia, shipping fever), foot rot, calf scours; as adjunctive therapy in septicemia accompanying mastitis and metritis.

(iii) *Limitations*. Administer at the rate of 1 gallon per 100 pounds of body weight per day for 4 days; as sodium sulfaethoxy-pyridazine; do not treat within 16 days of slaughter; as sole source of sulfonamide; for use by or on the order of a licensed veterinarian; milk that has been taken from animals during treatment and for 72 hours (6 milkings) after latest treatment must not be used for food.

§ 520.2240b Sulfaethoxy-pyridazine tablets.

(a) *Chemical name*. N-(6-Ethoxy-3-pyridazinyl) sulfanilamide.

(b) *Specifications*. Melting point range of 180° C to 186° C.

(c) *Sponsor*. See No. 010042 in § 510.600(c) of this chapter.

(d) *Related tolerances*. See § 556.650 of this chapter.

(e) *Conditions of use*. It is used for cattle as follows:

(1) *Amount*. 2.5 or 15 grams per tablet.

(i) *Indications for use*. Treatment of respiratory infections (pneumonia, shipping fever), foot rot, calf scours; as adjunctive therapy in septicemia accompanying mastitis and metritis.

(ii) *Limitations*. Administer 25 milligrams per pound of animal weight per day for 4 days; do not treat within 16 days of slaughter; as sole source of sulfonamide; milk that has been taken from animals during treatment and for 72 hours (6 milkings) after the latest treatment must not be used for food; for use only by or on the order of a licensed veterinarian.

(2) *Amount*. 15-gram controlled release tablets.

(i) *Indications for use*. Treatment of foot rot and respiratory infections (shipping fever and pneumonia)

caused by sulfonamide-susceptible pathogens (*E. coli*, streptococci, staphylococci, *Sphaerophorus necrophorus* and Gram-negative rods including *Pasteurella*); for use prophylactically in cattle during periods of stress for reducing losses due to sulfonamide sensitive disease conditions.

(ii) *Limitations*. Administer 100 milligrams per pound of body weight; do not treat within 16 days of slaughter; as sole source of sulfonamide; not for use in lactating dairy cows; Federal law restricts this drug to use by or on the order of a licensed veterinarian.

§ 520.2260 Sulfamethazine oral dosage forms.

§ 520.2260a Sulfamethazine tablets.

(a) *Sponsor*. See No. 010042 in § 510.600(c) of this chapter for use of 2.5-, 5-, or 15-gram sulfamethazine tablet.

(b) *Related tolerances in edible products*. See § 556.670 of this chapter.

(c) *Conditions of use*—(1) *Amount*. Administer as a single dose 100 milligrams of sulfamethazine per pound of body weight the first day and 50 milligrams per pound of body weight on each following day.

(2) *Indications for use*. For treatment of diseases caused by organisms sensitive to sulfamethazine.

(i) *Beef cattle and nonlactating dairy cattle*. Treatment of bacterial pneumonia and bovine respiratory disease complex (shipping fever complex) (*Pasteurella* spp.), colibacillosis (bacterial scours) (*Escherichia coli*), necrotic pododermatitis (foot rot) (*Fusobacterium necrophorum*), calf diphtheria (*Fusobacterium necrophorum*), acute mastitis (*Streptococcus* spp.), acute metritis (*Streptococcus* spp.), coccidiosis (*Eimeria bovis*, *Eimeria zurnii*).

(ii) *Horses*. Treatment of bacterial pneumonia (secondary infections associated with *Pasteurella* spp.), strangles (*Streptococcus equi*), and bacterial enteritis (*Escherichia coli*).

(3) *Limitations*. Administer daily until animal's temperature and appearance are normal. If symptoms persist after using for 2 or 3 days consult a veterinarian. Fluid intake must be adequate. Treatment should continue 24 to 48 hours beyond the remission of

disease symptoms, but not to exceed 5 consecutive days. Follow dosages carefully. Not for use in lactating dairy animals. Do not treat cattle within 10 days of slaughter. Not to be used in horses intended for food.

(d) *NAS/NRC status.* The conditions of use specified in this section have been reviewed by NAS/NRC and are found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

[47 FR 25321, June 11, 1982]

§ 520.2260b Sulfamethazine sustained-release boluses.

(a)(1) *Sponsor.* See No. 000859 in § 510.600(c) of this chapter for use of a 22.5-gram sulfamethazine prolonged-release bolus.

(2) *Conditions of use—(i) Amount.* Depending on the duration of therapeutic levels desired, administer boluses as a single dose as follows: 3½ days—1 bolus (22.5 grams) per 200 pounds of body weight; 5 days—1 bolus per 100 pounds of body weight.

(ii) *Indications for use.* Beef and nonlactating cattle for sustained treatment of shipping fever pneumonia caused or complicated by *Pasteurella multocida*; as an aid in the treatment of foot rot, mastitis, pneumonia, metritis, bacterial enteritis, calf diphtheria, and septicemia when caused or complicated by bacteria susceptible to sulfamethazine.

(iii) *Limitations.* Cattle that are acutely ill should be treated parenterally with a suitable antibacterial product to obtain immediate therapeutic blood levels; do not slaughter animals for food within 16 days of treatment; do not use in lactating dairy cattle; Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(b)(1) *Sponsor.* See No. 011519 in § 510.600(c) of this chapter for use of a 27-gram sulfamethazine sustained-release bolus.

(2) *Conditions of use—(i) Amount.* 27 grams (1 bolus) for each 150 pounds of body weight as a single dose.

(ii) *Indications for use.* For nonlactating cattle for the treatment of infections caused by organisms sensitive

to sulfamethazine such as hemorrhagic septicemia (shipping fever complex), bacterial pneumonia, foot rot, and calf diphtheria and as an aid in the control of bacterial diseases usually associated with shipping and handling of cattle.

(iii) *Limitations.* If no response within 2 to 3 days, reevaluate therapy; do not crush tablets; treated animals must not be slaughtered for food within 28 days after the latest treatment; Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(c)(1) *Sponsor.* See No. 053617 in § 510.600(c) of this chapter for use of a 32.1-gram sustained-release bolus.

(2) *Conditions of use—(i) Amount.* 32.1 grams (1 bolus) per 200 pounds of body weight.¹

(ii) *Indications for use.* For beef and nonlactating dairy cattle for the treatment of diseases caused by sulfamethazine-sensitive organisms as follows: bacterial pneumonia and bovine respiratory disease complex (shipping fever complex) caused by *Pasteurella* spp., colibacillosis (bacterial scours) caused by *E. coli*, necrotic pododermatitis (foot rot) and calf diphtheria caused by *Fusobacterium necrophorum*, and acute mastitis and acute metritis caused by *Streptococcus* spp.)¹

(iii) *Limitations.* After 72 hours, all animals should be reexamined for persistence of observable disease signs. If signs are present, consult a veterinarian. It is strongly recommended that a second dose be given to provide for an additional 72 hours of therapy, particularly in more severe cases. The dosage schedule should be used at each 72-hour interval. Animals should not receive more than 2 doses because of the possibility of incurring residue violations. This drug, like all sulfonamides, may cause toxic reactions and irreparable injury unless administered with adequate and continuous supervision; follow dosages carefully. Fluid intake must be adequate at all times throughout the 3-day therapy. Do not

¹ These conditions are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

use in lactating dairy cattle. Do not treat animals within 12 days of slaughter.

(d)(1) *Sponsor.* See 000859 in § 510.600(c) of this chapter for use of a 22.5-gram sulfamethazine sustained-release bolus.

(2) *Conditions of use—(i) Amount.* Administer 1 bolus (22.5 grams) per 200 pounds of body weight, as a single dose.

(ii) *Indications for use.* Beef and nonlactating dairy cattle for the prolonged treatment of the following diseases when caused by one or more of the listed pathogenic organisms sensitive to sulfamethazine: bovine respiratory disease complex (shipping fever complex) (*Pasteurella* spp.), bacterial pneumonia (*Pasteurella* spp.), necrotic pododermatitis (foot rot) (*Fusobacterium necrophorum*), colibacillosis (bacterial scours) (*Escherichia coli*), calf diphtheria (*Fusobacterium necrophorum*), acute mastitis (*Streptococcus* spp.) and acute metritis (*Streptococcus* spp.).

(iii) *Limitations.* Cattle that are acutely ill should be treated by injection with a suitable antibacterial product to obtain immediate therapeutic blood levels; do not slaughter animals for food within 16 days of treatment; do not use in lactating dairy cattle; if treated animals do not respond within 2 to 3 days, consult a veterinarian.

(e)(1) *Sponsor.* See No. 053617 in § 510.600(c) of this chapter for use of an 8.02-gram sulfamethazine sustained-release bolus.

(2) *Conditions of use—(i) Amount.* Administer 2 boluses (8.02 grams per bolus) per 100 pounds of body weight, as a single dose.

(ii) *Indications for use.* Administer orally to ruminating calves for the prolonged treatment of the following diseases when caused by one or more of the listed pathogenic organisms sensitive to sulfamethazine: bacterial pneumonia (*Pasteurella* spp.), colibacillosis (bacterial scours) (*E. coli*), and calf diphtheria (*Fusobacterium necrophorum*).

(iii) *Limitations.* For use in ruminating replacement calves only; 72 hours after dosing all animals should be re-examined for persistence of disease signs; if signs are present, consult a

veterinarian; do not slaughter animals for food for at least 12 days after the last dose; this product has not been shown to be effective for nonruminating calves; exceeding two consecutive doses may cause violative tissue residue to remain beyond the withdrawal time; do not use in calves under 1 month of age or calves being fed an all milk diet.

(f)(1) *Sponsor.* See No. 054273 in § 510.600(c) of this chapter for use of a 30-gram sulfamethazine sustained-release bolus.

(2) *Conditions of use—(i) Amount.* Administer at the rate of 1 bolus (30 grams per bolus) per 200 pounds of body weight, as a single dose.

(ii) *Indications for use.* Administer orally to beef cattle and nonlactating dairy cattle for the treatment of the following diseases when caused by one or more of the listed pathogenic organisms sensitive to sulfamethazine: bovine respiratory disease complex (shipping fever complex) associated with *Pasteurella* spp.; bacterial pneumonia associated with *Pasteurella* spp.; necrotic pododermatitis (foot rot) and calf diphtheria caused by *Fusobacterium necrophorum*; colibacillosis (bacterial scours) caused by *Escherichia coli*; coccidiosis caused by *Eimeria bovis* and *E. zurnii*; acute mastitis and metritis caused by *Streptococcus* spp.

(iii) *Limitations.* For use in beef cattle and nonlactating dairy cattle only; if symptoms persist for 2 or 3 days after use, consult a veterinarian; do not slaughter animals for food for at least 8 days after the last dose; do not use in lactating dairy cattle; do not administer more than two consecutive doses.

(g) *Related tolerances.* See § 556.670 of this chapter.

(Secs. 501, 502, 505, 701(a), 52 Stat. 1049-1053 as amended, 1055 (21 U.S.C. 351, 352, 355, 371(a)))

[46 FR 36132, July 14, 1981, as amended at 48 FR 18803, Apr. 26, 1983; 48 FR 32760, July 19, 1983; 49 FR 29057, July 18, 1984; 50 FR 49372, Dec. 2, 1985; 51 FR 30212, Aug. 25, 1986; 53 FR 40727, Oct. 18, 1988]

§ 520.2260c Sulfamethazine sustained-release tablets.

(a) *Sponsor.* See No. 011519 in § 510.600(c) of this chapter for use of

an 8-gram sulfamethazine sustained-release tablet.

(b) *Conditions of use*—(1) *Amount*. 8 grams (1 tablet) per 45 pounds of body weight as a single dose.

(2) *Indications for use*. In calves for sustained treatment of pneumonia caused by *Pasteurella* spp., colibacillosis (bacterial scours) caused by *Escherichia coli*; and calf diphtheria caused by *Fusobacterium necrophorum*.

(3) *Limitations*. If there is no response within 2 to 3 days, reevaluate therapy. Do not crush tablets. Treated animals must not be slaughtered for food within 18 days after the latest treatment. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[48 FR 28763, June 10, 1983]

§ 520.2261 Sulfamethazine sodium oral dosage forms.

[47 FR 25322, June 11, 1982]

§ 520.2261a Sulfamethazine sodium drinking water solution.

(a) *Sponsors*. See Nos. 017800 and 010042 in § 510.600(c) of this chapter for use of a 12.5-percent sulfamethazine sodium solution.

(b) *Related tolerances in edible products*. See § 556.670 of this chapter.

(c) *Conditions of use*—(1) *Amount*. Administer in drinking water to provide: Cattle and swine 112.5 milligrams of sulfamethazine sodium per pound of body weight per day on the first day and 56.25 milligrams per pound of body weight on subsequent days; Chickens, 61 to 89 milligrams of sulfamethazine sodium per pound of body weight per day, and turkeys 53 to 130 milligrams of sulfamethazine sodium per pound of body weight per day, depending upon the dosage, age, and class of chickens or turkeys, ambient temperature, and other factors.

(2) *Indications for use*. For treatment and control of diseases caused by organisms sensitive to sulfamethazine.

(i) *Beef and nonlactating dairy cattle*. Treatment of bacterial pneumonia and bovine respiratory disease complex (shipping fever complex) (*Pasteurella* spp.), colibacillosis (bacterial scours) (*Escherichia coli*), necrotic pododermatitis (foot rot) (*Fusobacter-*

tum necrophorum), calf diphtheria (*Fusobacterium necrophorum*), acute mastitis (*Streptococcus* spp.), and acute metritis (*Streptococcus* spp.).

(ii) *Swine*. Treatment of porcine colibacillosis (bacterial scours) (*Escherichia coli*), and bacterial pneumonia (*Pasteurella* spp.).

(iii) *Chickens and turkeys*. In chickens for control of infectious coryza (*Haemophilus gallinarum*), coccidiosis (*Eimeria tenella*, *Eimeria necatrix*), acute fowl cholera (*Pasteurella multocida*), and pullorum disease (*Salmonella pullorum*). In turkeys for control of coccidiosis (*Eimeria meleagridis*, *Eimeria adenoides*). Medicate as follows: Infectious coryza in chickens, medicate for 2 consecutive days; acute fowl cholera and pullorum disease, in chickens, medicate for 6 consecutive days; coccidiosis, in chickens and turkeys, medicate as in paragraph (c) of this section, then reduce amount of medication to one-half for 4 additional days.

(3) *Limitations*. Add the required dose to that amount of water that will be consumed in 1 day. Consumption should be carefully checked. Have only medicated water available during treatment. Withdraw medication from cattle, chickens, and turkeys 10 days prior to slaughter for food. Withdraw medication from swine 15 days before slaughter for food. Not for use in lactating dairy cattle. Do not medicate chickens or turkeys producing eggs for human consumption. Treatment of all diseases should be instituted early. Treatment should continue 24 to 48 hours beyond the remission of disease symptoms, but not to exceed a total of 5 consecutive days in cattle or swine. Medicated cattle, swine, chickens, and turkeys must actually consume enough medicated water which provides the recommended dosages.

(d) *NAS/NRC status*. The conditions of use specified in this section have been reviewed by NAS/NRC and are found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

[47 FR 25322, June 11, 1982, as amended at 47 FR 25735, June 15, 1982]

§ 520.2261b Sulfamethazine sodium soluble powder.

(a) *Sponsor.* See No. 010042 in § 510.600(c) of this chapter for use of a soluble powder composed of 100 percent sulfamethazine sodium.

(b) *Related tolerances in edible products.* See § 556.670 of this chapter.

(c) *Conditions of use.*—(1) *Amount.* Administer in drinking water to provide: Chickens 58 to 85 milligrams of sulfamethazine sodium per pound of body weight per day; turkeys 50 to 124 milligrams of sulfamethazine sodium per pound of body weight per day; depending upon the dosage, age, and class of chickens or turkeys, ambient temperature, and other factors. Administer to cattle and swine in drinking water, or as a drench, to provide 108 milligrams of sulfamethazine sodium per pound of body weight on the first day and 54 milligrams of sulfamethazine sodium per pound of body weight per day on the second, third, and fourth days of administration.

(2) *Indications for use.* For treatment and control of disease caused by organisms sensitive to sulfamethazine.

(i) *Beef and nonlactating dairy cattle.* Treatment of bacterial pneumonia and bovine respiratory disease complex (shipping fever complex) (*Pasteurella* spp.), colibacillosis (bacterial scours) (*Escherichia coli*), necrotic pododermatitis (foot rot) (*Fusobacterium necrophorum*), calf diphtheria (*Fusobacterium necrophorum*), acute mastitis (*Streptococcus* spp.), and acute metritis (*Streptococcus* spp.).

(ii) *Swine.* Treatment of porcine colibacillosis (bacterial scours) (*Escherichia coli*), and bacterial pneumonia (*Pasteurella* spp.).

(iii) *Chickens and turkeys.* In chickens for control of infectious coryza (*Haemophilus gallinarum*), coccidiosis (*Eimeria tenella*, *Eimeria necatrix*), acute fowl cholera (*Pasteurella multocida*), and pullorum disease (*Salmonella pullorum*). In turkeys for control of coccidiosis (*Eimeria meleagris*, *Eimeria adenoides*). Medicate as follows: Infectious coryza in chickens, medicate for 2 consecutive days; acute fowl cholera and pullorum disease in chickens, medicate for 6 consecutive days; coccidiosis in chickens and tur-

keys, medicate as in paragraph (c) of this section for 2 days, then reduce drug concentration to one-half for 4 additional days.

(3) *Limitations.* Add the required dose to that amount of water that will be consumed in 1 day. Consumption should be carefully checked. Have only medicated water available during treatment. Withdraw medication from cattle, chickens, and turkeys 10 days prior to slaughter for food. Withdraw medication from swine 15 days prior to slaughter for food. Not for use in lactating dairy animals. Do not medicate chickens or turkeys producing eggs for human consumption. Treatment of all diseases should be instituted early. Treatment should continue 24 to 48 hours beyond the remission of disease symptoms, but not to exceed a total of 5 consecutive days in cattle or swine. Medicated cattle, swine, chickens, and turkeys must actually consume enough medicated water which provides the recommended dosages.

(d) *NAS/NRC status.* The conditions of use specified in this section have been reviewed by NAS/NRC and are found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

[47 FR 25322, June 11, 1982]

§ 520.2280 Sulfamethizole and methenamine mandelate tablets.

(a) *Specifications.* Each tablet contains 250 milligrams of sulfamethizole and 250 milligrams of methenamine mandelate.

(b) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is indicated for the treatment of urinary tract infections in dogs and cats such as cystitis, nephritis, prostatitis, urethritis, and pyelonephritis. It is also used as an aid in the management of complications resulting from surgical manipulations of the urinary tract such as removal of calculi from the bladder, in ureterostomies, and in instrumentation of the urethra and bladder.

(2) It is administered at a dosage level of one tablet for each 20 pounds

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of body weight given three times per day. The drug should be given until all signs are alleviated. To reduce the possibility of a relapse, it is suggested that therapy be continued for a further period of a week to 10 days.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13838, Mar. 27, 1975, as amended at 50 FR 13561, Apr. 5, 1985]

§ 520.2320 Sulfanitrin and aklomide in combination.

(a) *Chemical names.* (1) Sulfanitrin: Acetyl-(*p*-nitrophenyl)-sulfanilamide.

(2) Aklomide: 2-Chloro-4-nitrobenzamide.

(b) *Specifications.* (1) Sulfanitrin conforms to the following specifications:

(i) Melting point range: 260° C. to 261° C.

(ii) Assay (by sodium nitrite titration): 97 to 100.5 percent.

(iii) Moisture (Method No. 6.123, "Toluene Distillation Method—Official Final Action" in "Official Methods of Analysis of the Association of Official Analytical Chemists," 13th Ed., 1980, p. 83. Copies are available from the Association of Official Analytical Chemists, P.O. Box 540, Benjamin Franklin Station, Washington, D.C. 20044, or available for inspection at the Office of the Federal Register, 1100 L St. NW., Washington, D.C. 20408): Not more than 2.0 percent.

(iv) Molecular weight: 335.34.

(v) Soluble in 0.1*N* sodium hydroxide, reprecipitating unchanged on acidification.

(2) Aklomide conforms to the following specifications:

(i) Minimum melting point: 170° C.

(ii) Moisture content: Not to exceed 1.0 percent.

(iii) Purity: Not less than 98 percent on an anhydrous basis.

(c) *Sponsor.* See No. 017210 in § 510.600(c) of this chapter.

(d) *Related tolerances.* See §§ 556.30 and 556.680 of this chapter.

(e) *Conditions of use.* It is used in the drinking water of chickens as follows:

(1) *Amount.* 374-747 milligrams of sulfanitrin with 477-954 milligrams of aklomide.

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(2) *Indications for use.* As an aid in the treatment of coccidiosis caused by *E. tenella*, *E. necatrix*, and *E. acervulina*.

(3) *Limitations.* Administer for 2 days at 747 milligrams of sulfanitrin per gallon and 954 milligrams of aklomide per gallon, followed by 5 days at 374 milligrams of sulfanitrin per gallon and 477 milligrams of aklomide per gallon; do not treat birds over 6 weeks of age; do not administer within 5 days of slaughter; not for laying chickens.

[40 FR 13838, Mar. 27, 1975, as amended at 47 FR 9396, Mar. 5, 1982]

§ 520.2325 Sulfaquinoxaline oral dosage forms.

[48 FR 3964, Jan. 28, 1983]

§ 520.2325a Sulfaquinoxaline drinking water.

(a)—(b) [Reserved]

(c) *Sponsor.* (1) Use of a 25-percent soluble powder and a 20-percent solution has been granted to No. 000006 in § 510.600(c) of this chapter for use as provided for in paragraph (e) of this section.

(2) Use of 3.44-percent and 12.85-percent solutions has been granted to No. 017800 in § 510.600(c) of this chapter for use as provided for in paragraphs (e) (1), (2), (3), (4)(i), and (4)(ii) of this section.

(d) *NAS/NRC status.* The conditions of use specified in this section have been reviewed by NAS/NRC and are found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency information. Applications must be accompanied by a written commitment to undertake the human safety studies required by FDA.

(e) *Conditions of use.* It is used in drinking water as follows:

(1) *Chickens.* (i) As an aid in the control of outbreaks of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, and *E. brunetti*.

(ii) Administer at the 0.04 percent level for 2 or 3 days, skip 3 days then administer at the 0.025 percent level for 2 more days. If bloody droppings

appear, repeat treatment at the 0.025 percent level for 2 more days. Do not change litter unless absolutely necessary. Do not give flushing mash.

(2) *Turkeys.* (i) As an aid in the control of outbreaks of coccidiosis caused by *Eimeria meleagridis* and *E. adenoeides*.

(ii) Administer at the 0.025 percent level for 2 days, skip 3 days, give for 2 days, skip 3 days and give for 2 more days. Repeat if necessary. Do not change litter unless absolutely necessary. Do not give flushing mash.

(3) *Chickens and turkeys.* (i) As an aid in the control of acute fowl cholera caused by *Pasteurella multocida* susceptible to sulfaquinoxaline and fowl typhoid caused by *Salmonella gallinarum* susceptible to sulfaquinoxaline.

(ii) Administer at the 0.04 percent level for 2 or 3 days. Move birds to clean ground. If disease recurs, repeat treatment. If cholera has become established as the respiratory or chronic form, use feed medicated with sulfaquinoxaline. Poultry which have survived typhoid outbreaks should not be kept for laying house replacements or breeders unless tests show they are not carriers.

(4) *Cattle and calves.* (i) For the control and treatment of outbreaks of coccidiosis caused by *Eimeria bovis* or *E. zurnii*.

(ii) Administer at the 0.015-percent level for 3 to 5 days in drinking water medicated with sulfaquinoxaline solution.

(iii) In lieu of treatment as provided in paragraph (e)(4)(ii) of this section, administer 1 teaspoon of 25-percent sulfaquinoxaline soluble powder per day for each 125 pounds of body weight for 3 to 5 days in drinking water.

(f) *Limitations.* Consult a veterinarian or poultry pathologist for diagnosis. May cause toxic reactions unless the drug is evenly mixed in water at dosages indicated and used according to directions. For control of outbreaks of disease, medication should be initiated as soon as the diagnosis is determined. Medicated chickens, turkeys, cattle, and calves must actually consume enough medicated water which provides a recommended dosage of ap-

proximately 10 to 45 milligrams per pound per day in chickens, 3.5 to 55 milligrams per pound per day in turkeys, and approximately 6 milligrams per pound per day in cattle and calves depending on the age, class of animal, ambient temperature, and other factors. Not for use in lactating dairy cattle. Do not give to chickens, turkeys or cattle within 10 days of slaughter for food. Do not medicate chickens or turkeys producing eggs for human consumption. Make fresh drinking water daily.

[48 FR 3964, Jan. 28, 1983, as amended at 48 FR 26762, June 10, 1983]

§ 520.2325b Sulfaquinoxaline drench.

(a)–(b) [Reserved]

(c) *Sponsor.* See No. 000006 in § 510.600(c) of this chapter.

(d) *NAS/NRC status.* The conditions of use specified in this section have been reviewed by NAS/NRC and are found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency information. Applications must be accompanied by a written commitment to undertake the human safety studies required by FDA.

(e) *Conditions of uses.* As a 25-percent sulfaquinoxaline soluble powder.

(1) For the control and treatment of outbreaks of coccidiosis in cattle and calves caused by *Eimeria bovis* or *E. zurnii*.

(2) Give one teaspoon of 25 percent sulfaquinoxaline soluble powder for each 125 pounds of body weight for 3 to 5 days as a drench.

(f) *Limitations.* For control of outbreaks of disease, medication should be initiated as soon as the diagnosis is determined. Consult a veterinarian for diagnosis. Do not give to cattle within 10 days of slaughter for food. Not for use in lactating dairy cattle.

[48 FR 3964, Jan. 28, 1983]

§ 520.2330 Sulfisoxazole tablets.

(a) *Specifications.* Each tablet contains 260 milligrams (4 grains) of sulfisoxazole.

(b) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(c) *Conditions of use*—(1) *Amount*. Administer one tablet orally per 4 pounds of body weight.¹

(2) *Indications for use*. Use in dogs and cats as an aid in treatment of bacterial pneumonia and bacterial enteritis when caused by organisms sensitive to sulfoxazole.¹

(3) *Limitations*. Repeat dosage at 24-hour intervals until 2 to 3 days after disappearance of clinical symptoms. (Administration of one-half daily dosage at 12-hour intervals or one-third daily dosage at 8-hour intervals will provide a more constant blood level.) Provide adequate supply of drinking water. If symptoms persist after using this preparation for 2 or 3 days, consult a veterinarian.¹

[43 FR 60895, Dec. 29, 1978]

§ 520.2362 Thienium closylate tablets.

(a) *Chemical name*. (N,N-Dimethyl-N-2-phenoxyethyl-N-2'-thenylammonium)-p-chlorobenzene-sulfonate.

(b) *Specifications*. Thienium closylate tablets contain thienium closylate equivalent to 500 milligrams thienium as base in each tablet.

(c) *Sponsor*. See No. 017220 in § 510.600(c) of this chapter.

(d) *Conditions of use*. (1) The tablets are administered orally to dogs as a single day treatment of canine ancylostomiasis by the removal from the intestines of the adult forms of the species *Ancylostoma caninum* and *Uncinaria stenocephala* (hookworms). Dogs weighing 10 pounds and over are administered 1 tablet as a single dose. Dogs weighing 5 to 10 pounds are administered one-half tablet twice during a single day. All dosages are given for 1 day only. The treatment should be repeated after 2 or 3 weeks.

(2) Suckling puppies or recently weaned puppies weighing less than 5 pounds should not be treated with the drug. Animals that are severely infected, exhibiting evidence of intestinal hemorrhage, debilitation, and anemia, should be given supportive treatment.

¹ These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13838, Mar. 27, 1975, as amended at 41 FR 53477, Dec. 7, 1976; 46 FR 48642, Oct. 2, 1981]

§ 520.2380 Thiabendazole oral dosage forms.

§ 520.2380a Thiabendazole top dressing and mineral protein feed block.

(a) *Chemical name*. 2-(4-Thiazolyl)-benzimidazole.

(b) *Specifications*. Conforms to N.F. XII.

(c) *Sponsor*. (1) See No. 017800 in § 510.600(c) of this chapter for the sponsor of the usage provided by paragraph (e)(1)(ii) of this section.

(2) See No. 000006 in § 510.600(c) of this chapter for the sponsor of the usages provided for by paragraph (e)(1)(ii) of this section.

(3) See No. 021930 in § 510.600(c) of this chapter for the sponsor of the usage provided for by paragraph (e)(2) of this section.

(d) *Related tolerances*. See § 556.730 of this chapter.

(e) *Conditions of use*. It is used as follows:

(1) *Horses*—(i) *Route of administration*. In feed, as a top dressing.

(a) *Amount*. 2 grams per 100 pounds of body weight.

(b) *Indications for use*. For control of large strongyles, small strongyles, pinworms, and threadworms (including members of the genera *Strongylus*, *Cyathostomum*, *Cylicobrachytus*, and related genera, *Craterostomum*, *Oesophagodontus*, *Poteriostomum*, *Oxyuris*, and *Strongyloides*).

(c) *Limitations*. Add to the usual feed of horses mixed into that amount of the feed normally consumed at one feeding. Warning: Not for use in horses intended for food.

(ii) *Route of administration*. In feed.

(a) *Amount*. 2 grams per 100 pounds of body weight.

(1) *Indications for use*. For control of large and small strongyles, *Strongyloides*, and pinworms of the genera *Strongylus*, *Cyathostomum*, *Cylicobrachytus* and related genera, *Craterosto-*

mum, *Oesophagodontus*, *Poteriostomum*, *Oxyuris*, and *Strongyloides*.

(2) *Limitations*. Administer in a single dosage mixed with the normal grain ration given at one feeding. Warning: Not for use in horses intended for food.

(b) *Amount*. 4 grams per 100 pounds of body weight.

(1) *Indications for use*. For control of ascarids of the genus *Parascaris*.

(2) *Limitations*. Administer in a single dosage mixed with the normal grain ration given at one feeding. Warning: Not for use in horses intended for food.

(2) *Cattle*—(i) *Route of administration*. In feed block.

(ii) *Amount*. 3.3 percent block consumed at the recommended level of 0.11 pound per 100 pounds of body weight per day.

(iii) *Indications for use*. For control of infections of gastrointestinal roundworms (*Trichostrongylus*, *Haemonchus*, *Ostertagia* and *Cooperia*).

(iv) *Limitations*. Administer to cattle on pasture or range accustomed to mineral protein block feeding for 3 days. Milk taken from animals during treatment and within 96 hours (8 milkings) after the latest treatment must not be used for food. Do not treat cattle within 3 days of slaughter. For a satisfactory diagnosis, a microscopic fecal examination should be performed by a veterinarian or diagnostic laboratory prior to worming. Animals maintained under conditions of constant worm exposure may require re-treatment within 2 to 3 weeks. Animals that are severely parasitized, sick, or off feed should be isolated and a veterinarian consulted for advice concerning treatment.

[40 FR 13838, Mar. 27, 1975, as amended at 41 FR 9149, Mar. 3, 1976]

§ 520.2380b Thiabendazole drench or oral paste.

(a) *Chemical name*. 2-(4-Thiazolyl) benzimidazole.

(b) *Specifications*. Conforms to N.F. XII.

(c) *Sponsor*. See No. 000006 in § 510.600(c) of this chapter for the sponsor of the usages provided for by paragraph (e) of this section.

(d) *Related tolerances*. See § 556.730 of this chapter.

(e) *Conditions of use*. It is used as follows:

(1) *Horses*. As a single liquid oral dose, administered as a drench or by stomach tube; or as an oral paste.

(i) *Amount*. 2 grams per 100 pounds of body weight.

(a) *Indications for use*. For the control of infections of large strongyles (*Strongylus vulgaris*, *Strongylus edentatus*), small strongyles (*Cyathostomum*, *Cylicobrachytus* and related genera, *Craterostomum*, *Oesophagodontus*, *Poteriostomum*), pinworms (*Oxyuris*), and threadworms (*Strongyloides*).

(b) *Limitations*. Not for use in horses to be slaughtered for food purposes. When administered by stomach tube, for use only by or on the order of a licensed veterinarian. When for use as a liquid oral drench or an oral paste, consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

(ii) *Amount*. 4 grams per 100 pounds of body weight.

(a) *Indications for use*. For control of infections of ascarids (*Parascaris*).

(b) *Limitations*. Not for use in horses to be slaughtered for food purposes. When administered by stomach tube, use only by or on the order of a licensed veterinarian. When for use as a liquid oral drench or an oral paste, consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

(2) *Pigs*. As an oral paste.

(i) *Amount*. 200 milligrams for each 5 to 7 pounds of body weight per dose.

(ii) *Indications for use*. For control of infections with *Strongyloides ransomi*. These infections are commonly found in Southeastern United States.

(iii) *Limitations*. Administer to baby pigs (1 to 8 weeks of age). Treatment may be repeated in 5 to 7 days if necessary. Before treatment, obtain an accurate diagnosis from a veterinarian or diagnostic laboratory. Do not treat within 30 days of slaughter.

(3) *Cattle*. Orally as a drench and in paste form using a dosing gun designed for the product.

(i) *Amount*. 3 grams per 100 pounds of body weight.

(a) *Indications for use.* Control of infections of gastrointestinal roundworms (*Trichostrongylus* spp., *Haemonchus* spp., *Nematodirus* spp., *Ostertagia* spp., and *Oesophagostomum radiatum*).

(b) *Limitations.* For most effective results, severely parasitized animals or those constantly exposed to helminth infection should be re-treated every 2 to 3 weeks. Milk taken from treated animals within 96 hours (8 milkings) after the latest treatment must not be used for food. Do not treat cattle within 3 days of slaughter. For a satisfactory diagnosis, a microscopic fecal examination should be performed prior to worming.

(i) *Amount.* 5 grams per 100 pounds of body weight.

(a) *Indications for use.* Control of infections of *Cooperia* spp. or severe infections of other species in paragraph (e)(3)(i)(a) of this section.

(b) *Limitations.* For most effective results, severely parasitized animals or those constantly exposed to helminth infection should be re-treated every 2 to 3 weeks. Milk taken from treated animals within 96 hours (8 milkings) after the latest treatment must not be used for food. Do not treat cattle within 3 days of slaughter. For a satisfactory diagnosis, a microscopic fecal examination should be performed prior to worming.

(4) *Sheep and goats.* Orally, as a drench.

(i) *Amount.* 2 grams per 100 pounds of body weight.

(ii) *Indications for use.* Control of infections of gastrointestinal roundworms in sheep and goats. (*Trichostrongylus* spp., *Haemonchus* spp., *Ostertagia* spp., *Cooperia* spp., *Nematodirus* spp., *Bunostomum* spp., *Strongyloides* spp., *Chabertia* spp., and *Oesophagostomum* spp.); also active from 3 hours to 3 days following treatment against ova and larvae passed by sheep (good activity against *Trichostrongylus colubriformis* and *axei*, *Ostertagia* spp., *Bunostomum* spp., *Nematodirus* spp., and *Strongyloides* spp.; less effective against *Haemonchus contortus* and *Oesophagostomum* spp.).

(iii) *Limitations.* As a single oral dose; do not treat animals within 30 days of slaughter; milk taken from

treated animals within 96 hours (8 milkings) after the latest treatment must not be used for food; in severe infections in sheep, treatment should be repeated in 2 to 3 weeks.

(5) *Goats.* Orally, as a drench.

(i) *Amount.* 3 grams per 100 pounds of body weight.

(ii) *Indications for use.* Control of severe infections of gastrointestinal roundworms (*Trichostrongylus* spp., *Haemonchus* spp., *Ostertagia* spp., *Cooperia* spp., *Nematodirus* spp., *Bunostomum* spp., *Strongyloides* spp., *Chabertia* spp., and *Oesophagostomum* spp.).

(iii) *Limitations.* As a single oral dose; do not treat animals within 30 days of slaughter; milk taken from treated animals within 96 hours (8 milkings) after the latest treatment must not be used for food; treatment should be repeated in 2 to 3 weeks.

[40 FR 13838, Mar. 27, 1975, as amended at 41 FR 9149, Mar. 3, 1976; 41 FR 47424, Oct. 29, 1976]

§ 520.2380c Thiabendazole bolus.

(a) *Chemical name.* 2-(4-Thiazolyl) benzimidazole.

(b) *Specifications.* Conforms to N.F. XII.

(c) *Sponsor.* See No. 000006 in § 510.600(c) of this chapter.

(d) *Related tolerances.* See § 556.730 of this chapter.

(e) *Conditions of use.* It is used as follows:

(1) *Cattle.* In a bolus.

(i) *Amount.* 3 grams per 100 pounds of body weight.

(a) *Indications for use.* Control of infections of gastrointestinal roundworms (general *Trichostrongylus* spp., *Haemonchus* spp., *Nematodirus* spp., *Ostertagia* spp., and *Oesophagostomum radiatum*).

(b) *Limitations.* As a single oral dose; may repeat once in 2 to 3 weeks; do not treat animals within 3 days of slaughter; milk taken from treated animals within 96 hours (8 milkings) after the latest treatment must not be used for food.

(ii) *Amount.* 5 grams per 100 pounds of body weight.

(a) *Indications for use.* Control of severe infections of gastrointestinal

roundworms (genera *Trichostrongylus* spp., *Haemonchus* spp., *Nematodirus* spp., *Ostertagia* spp., and *Oesophagostomum radiatum*). Control of infections with *Cooperia* spp.

(b) *Limitations*. As a single oral dose; as a drench or bolus; may repeat once in 2 to 3 weeks; do not treat animals within 3 days of slaughter; milk taken from treated animals within 96 hours (8 milkings) after the latest treatment must not be used for food.

(2) *Sheep and goats*. In a bolus.

(i) *Amount*. 2 grams per 100 pounds of body weight.

(ii) *Indications for use*. Control of infections of gastrointestinal roundworms in sheep and goats (general *Trichostrongylus* spp., *Haemonchus* spp., *Ostertagia* spp., *Cooperia* spp., *Nematodirus* spp., *Bunostomum* spp., *Strongyloides* spp., *Chabertia* spp., and *Oesophagostomum* spp.); also active from 3 hours to 3 days following treatment against ova and larvae passed by sheep (good activity against *T. colubriformis* and *azei*, *Ostertagia* spp., *Bunostomum* spp., *Nematodirus* spp., and *Strongyloides* spp.; less effective against *Haemonchus contortus* and *Oesophagostomum* spp.).

(iii) *Limitations*. As a single oral dose; do not treat animals within 30 days of slaughter; milk taken from treated animals within 96 hours (8 milkings) after the latest treatment must not be used for food; in severe infections in sheep, treatment should be repeated in 2 to 3 weeks.

(3) *Goats*. In a bolus.

(i) *Amount*. 3 grams per 100 pounds of body weight.

(ii) *Indications for use*. Control of severe infections of gastrointestinal roundworms (genera *Trichostrongylus* spp., *Haemonchus* spp., *Ostertagia* spp., *Cooperia* spp., *Nematodirus* spp., *Bunostomum* spp., *Strongyloides* spp., *Chabertia* spp., and *Oesophagostomum* spp.).

(iii) *Limitations*. As a single oral dose; do not treat animals within 30 days of slaughter; milk taken from treated animals within 96 hours (8 milkings) after the latest treatment must not be used for food; treatment should be repeated in 2 to 3 weeks.

(40 FR 13838, Mar. 27, 1975, as amended at 41 FR 9149, Mar. 3, 1976)

§ 520.2380d Thiabendazole, piperazine citrate suspension.

(a) *Specifications*. Each fluid ounce of suspension contains 2 grams of thiabendazole and 2.5 grams of piperazine (from piperazine citrate).

(b) *Sponsor*. See No. 000006 in § 510.600(c) of this chapter.

(c) *Conditions of use*. (1) It is administered to horses by stomach tube or as a drench at the rate of 1 fluid ounce of suspension per 100 pounds of body weight for the control of large strongyles, small strongyles, pinworms, *Strongyloides* and ascarids (including members of the genera *Strongylus* spp., *Cyathostomum* spp., *Cylicobrachytus* spp. and related genera *Craterostomum* spp., *Oesophagodontus* spp., *Poteriostomum* spp., *Oxyuris* spp., *Strongyloides* spp., and *Parascaris* spp.).

(2) Do not use in horses intended to be used for food purposes.

(3) For use by or on the order of a licensed veterinarian.

§ 520.2380e Thiabendazole with trichlorfon.

(a) *Specifications*. The drug contains 5 grams of thiabendazole with 4.5 grams of trichlorfon, or 20 grams of thiabendazole with 18 grams of trichlorfon.

(b) *Sponsor*. See No. 017135 in § 510.600(c) of this chapter.

(c) *Conditions of use*. (1) Used for the treatment and control of bots (*Gasterophilus* spp.), large strongyles (*Strongylus* spp.), small strongyles (genera *Cyathostomum*, *Cylicobrachytus*, *Craterostomum*, *Oesophagodontus*, *Poteriostomum*), pinworms (*Oxyuris* spp., *Strongyloides* spp.), and ascarids (*Parascaris* spp.) in horses.

(2) Administer 2 grams of thiabendazole with 1.8 grams of trichlorfon per 100 pounds of body weight sprinkled on the animals' usual daily ration of feed, or may be mixed in 5 to 10 fluid ounces of water and administered by stomach tube or drench.

(3) Do not re-treat more than once every 30 days, preferably every 6 to 8 weeks.

(4) Do not treat animals if sick or debilitated; less than 4 months of age; or mares in last month of pregnancy.

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(5) Do not administer intravenous anesthetics, especially muscle relaxants, within 2 weeks of use.

(6) Not for animals intended for food use.

(7) Do not use within a few days before or after treatment with or exposure to cholinesterase-inhibiting drugs, pesticides, or chemicals.

(8) If the label bears directions for administration of the drug by stomach tube or drench it shall also bear the statement: Caution; Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 23071, May 28, 1975, as amended at 48 FR 48229, Oct. 18, 1983]

§ 520.2380f Thiabendazole, piperazine phosphate powder.

(a) *Specifications.* Each ounce of water dispersible powder contains 6.67 grams of thiabendazole and 8.33 grams of piperazine (as piperazine phosphate).

(b) *Sponsor.* See No. 000006 in § 510.600(c) of this chapter.

(c) *Conditions of use.*—(1) *Amount.* 2 grams of thiabendazole and 2.5 grams of piperazine (0.3 ounce of powder) per 100 pounds of body weight.

(2) *Indications for use.* Treatment of infections of large strongyles (genus *Strongylus*), small strongyles (genera *Cyathostomum*, *Cylicobrachytus*, and related genera *Craterostomum*, *Oesophagodontus*, *Poteriostomum*), pinworms (*Oxyuris*), threadworms (*Strongyloides*), and ascarids (*Parascaris*) in horses.

(3) *Limitations.* Use a single oral dose. Administer as a drench or by stomach tube suspended in 1 pint of warm water; by dose syringe suspended in ½ ounce of water for each 100 pounds of body weight; or sprinkled over a small amount of daily feed. Not for animals intended for food use. If the label bears directions for administration by stomach tube or drench, it shall also bear the statement "Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian;" if not labeled for use by stomach tube or drench, the label shall bear the statement, "Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism."

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[48 FR 18963, Mar. 27, 1981, as amended at 46 FR 52330, Oct. 27, 1981]

§ 520.2455 Tiamulin.

(a) *Specifications.* A water-soluble powder containing 45 percent tiamulin used to make a medicated drinking water containing 227 or 677 milligrams of tiamulin per gallon.

(b) *Sponsor.* See No. 054273 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See § 556.738 of this chapter.

(d) *Conditions of use in swine.*—(1) *Amount.* 3.5 milligrams of tiamulin per pound of body weight for 5 days.

(i) *Indications for use.* For treatment of swine dysentery associated with *Treponema hyodysenteriae* susceptible to tiamulin.

(ii) *Limitations.* Use for 5 consecutive days. Withdraw 3 days before slaughter. Prepare fresh water daily. Not for use in swine over 250 pounds body weight. Use as only source of drinking water.

(2) *Amount.* 10.5 milligrams of tiamulin per pound of body weight for 5 days.

(i) *Indications for use.* For treatment of swine pneumonia due to *Haemophilus pleuropneumoniae* susceptible to tiamulin.

(ii) *Limitations.* Use for 5 consecutive days. Withdraw 7 days before slaughter. Prepare fresh water daily. Not for use in swine over 250 pounds body weight. Use as only source of drinking water. Do not allow consumption of feeds containing polyether ionophores (e.g., monensin, lasalocid, or salinomycin) as adverse reactions may occur.

[52 FR 15718, Apr. 30, 1987]

§ 520.2460 Ticarbodine oral dosage forms.

§ 520.2460a Ticarbodine tablets.

(a) *Specifications.* Ticarbodine tablets, veterinary contain 90, 225, or 900 milligrams of ticarbodine per tablet.

(b) *Sponsor.* See No. 000986 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used in dogs for the removal of roundworms (*Toxocara canis*), hookworms (*Ancylostoma caninum* and *Uncinaria stenocephala*), and tapeworms (*Dipyl-*

dium caninum and *Taenia pisiformis*).

(2) Dosage is administered at 45 milligrams of the drug per pound of body weight in a single dose. Dosage may be repeated in 21 days.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

§ 520.2460b Ticarbodine capsules.

(a) *Specifications*. Each capsule contains 90, 225, 450, or 900 milligrams of ticarbodine.

(b) *Sponsor*. See No. 000986 in § 510.600(c) of this chapter.

(c) *Conditions of use*. (1) The drug is used in dogs for removal of roundworms (*Toxocara canis*), hookworms (*Ancylostoma caninum* and *Uncinaria stenocephala*), and tapeworms (*Dipylidium caninum* and *Taenia pisiformis*).

(2) Dosage is administered orally as a single dose at 45 milligrams per lb. of body weight. Dosage may be repeated at 21-day intervals.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

§ 520.2473 Tioxidazole oral dosage forms.

[50 FR 52772, Dec. 26, 1985]

§ 520.2473a Tioxidazole granules.

(a) *Specifications*. Each gram of granules contains 200 milligrams of tioxidazole.

(b) *Sponsor*. See No. 000061 in § 510.600(c) of this chapter.

(c) *Conditions of use*—(1) *Horses*—(i) *Amount*. 5 milligrams per pound of body weight as a single dose.

(ii) *Indications for use*. Removal of mature large strongyles (*Strongylus edentatus*, *S. equinus*, and *S. vulgaris*), mature ascarids (*Parascaris equorum*), mature and immature (4th larval stage) pinworms (*Oxyuris equi*), and mature small strongyles (*Triodontophorus* spp.).

(iii) *Limitations*. For administration with feed: Sprinkle required amount of granules on a small amount of the usual grain ration and mix. Prepare for each horse individually. Withholding of feed or water not necessary. Not for use in horses intended for food. The reproductive safety of tioxidazole

in breeding animals has not been determined. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism. It is recommended that this drug be administered with caution to sick or debilitated horses.

(2) [Reserved]

[50 FR 52772, Dec. 26, 1985; 51 FR 2693, Jan. 21, 1986, as amended at 52 FR 7832, Mar. 13, 1987]

§ 520.2473b Tioxidazole paste.

(a) *Specifications*. Each plastic syringe contains 6.25 grams of tioxidazole.

(b) *Sponsor*. See No. 000061 in § 510.600(c) of this chapter.

(c) *Conditions of use*—(1) *Horses*—(i) *Amount*. 5 milligrams of tioxidazole per pound of body weight as a single dose.

(ii) *Indications for use*. Removal of mature large strongyles (*Strongylus edentatus*, *S. equinus*, and *S. vulgaris*), mature ascarids (*Parascaris equorum*), mature and immature (4th larval stage) pinworms (*Oxyuris equi*), and mature small strongyles (*Triodontophorus* spp.).

(iii) *Limitations*. Administer orally by inserting the nozzle of the syringe through the space between front and back teeth and deposit the required dose on the base of the tongue. Before dosing, make sure the horse's mouth contains no feed. Not for use in horses intended for food. The reproductive safety of tioxidazole in breeding animals has not been determined. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism. It is recommended that this drug be administered with caution to sick or debilitated horses.

(2) [Reserved]

[52 FR 43059, Nov. 9, 1987]

§ 520.2480 Triamcinolone tablets.

(a) *Specifications*. Each tablet contains 0.5 milligram of the drug.

(b) *Sponsor*. See No. 000859 in § 510.600(c) of this chapter.

(c) *NAS/NRC status*. The conditions of use specified in this section are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as speci-

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fied by § 514.111 of this chapter, but may require bioequivalency and safety information.

(d) *Conditions of use.* (1) The drug is indicated for use in dogs and cats for its anti-inflammatory activity.

(2) The dosage range for dogs is 0.25 milligram to 2.0 milligrams per day for 7 days and the dosage range for cats is 0.25 milligram to 0.5 milligram per day for 7 days. Daily dosage may be given in two or more divided doses. Dosage must be adjusted to the response of the individual animal. Generally, initial dosages are at the higher range and when the response is satisfactory, the dosage is gradually reduced until a minimum adequate dose is obtained. Dosage may be repeated when necessary. Daily dosage may be given in two or more divided doses.

(3) The labeling shall comply with the requirements of § 510.410 of this chapter.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13838, Mar. 27, 1975, as amended at 51 FR 26002, July 18, 1986]

§ 520.2481 Triamcinolone acetonide tablets.

(a) *Specifications.* Each tablet contains either 0.5 milligram or 1.5 milligrams of the drug.

(b) *Sponsor.* See Nos. 053501 and 054273 in § 510.600(c) of this chapter.

(c) *NAS/NRC status.* The conditions of use specified in this section are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(d) *Conditions of use.* (1) The drug is indicated for use in dogs and cats for its anti-inflammatory activity.

(2) An initial daily dosage of 0.05 milligram per pound of body weight is usually sufficient to control symptoms, although up to 0.1 milligram per pound of body weight may be given daily if response to the smaller dose is inadequate. As soon as feasible, and in any case within 2 weeks, dosage should be reduced gradually to maintenance levels of 0.0125 to 0.025 milligram per pound of body weight per day. Ther-

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apy should be discontinued by a gradual reduction in dosage after the condition has been controlled for several days. Therapy may be initiated with a single dose of sterile triamcinolone acetonide suspension veterinary in which case the tablet dosage should be administered beginning 5 to 7 days after the injection or when symptoms reappear.

(3) The labeling shall comply with the requirements of § 510.410 of this chapter.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13838, Mar. 27, 1975, as amended at 51 FR 26002, July 18, 1986; 53 FR 40727, Oct. 18, 1988]

§ 520.2482 Triamcinolone acetonide oral powder.

(a) *Specifications.* Each 15 grams of triamcinolone acetonide oral powder contains 10 milligrams of triamcinolone acetonide.

(b) *Sponsor.* See No. 053501 in § 510.600(c) of this chapter.

(c) *NAS/NRC status.* The conditions of use specified in this section are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(d) *Conditions of use.* (1) The drug is used as an anti-inflammatory agent for horses.

(2) It is administered at a dosage of 0.005 to 0.01 milligram triamcinolone acetonide per pound of body weight twice daily, sprinkled (top-dressed) on a small portion of feed. Treatment may be initiated with a single dose of sterile triamcinolone acetonide suspension USP followed after 3 or 4 days with the use of triamcinolone acetonide oral powder.

(3) The labeling shall comply with the requirements of § 510.410 of this chapter.

(4) Not for use in horses intended for food.

(5) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

Food and Drug Administration, HHS

§ 520.2520c

[41 FR 24884, June 21, 1976, as amended at 50 FR 41489, Oct. 11, 1985; 51 FR 26002, July 18, 1986]

§ 520.2520 Trichlorfon oral dosage forms.

§ 520.2520a Trichlorfon oral.

(a) **Chemical name.** Dimethyl 2,2,2-trichloro-1-hydroxyethyl phosphonate.

(b) **Sponsor.** See Nos. 017800 and 000859 in § 510.600(c) of this chapter.

(c) **Special considerations.** This drug is a cholinesterase inhibitor. Do not use this product on animals simultaneously or within a few days before or after treatment with or exposure to cholinesterase-inhibiting drugs, pesticides, or chemicals.

(d) **Conditions of use.** (1) It is intended for use in horses for the removal of bots (*Gasterophilus spp.*), ascarids (*Parascaris equorum*), and pinworms (*Oxyuris equi*).

(2) Mix the drug, either dry or dissolved in water, in feed and administer at the rate of 4.5 grams of trichlorfon per 250 pounds of body weight. The drug is to be consumed at one feeding. Treatment should be repeated at 3-to 4-month intervals. Do not repeat treatment more frequently than every 30 days. Do not treat horses to be used for food. Do not treat sick or debilitated horses, colts under 4 months of age, mares in the last month of pregnancy, or animals other than horses. Do not administer intravenous anesthetics, especially muscle relaxants, for a period of 2 weeks after treatment.

[40 FR 13838, Mar. 27, 1975, as amended at 44 FR 63097, Nov. 2, 1979]

§ 520.2520b Trichlorfon and atropine.

(a) **Chemical name.** (1) For trichlorfon: O,O-Dimethyl 2,2,2-trichloro-1-hydroxyethyl phosphonate.

(2) For atropine: Atropine N.F.

(b) **Sponsor.** See No. 000856 in § 510.600(c) of this chapter.

(c) **Conditions of use.** (1) The drug is used for the treatment of *Syphacia obvelata* (pinworm) in laboratory mice.

(2) It is administered in distilled water as sole source of drinking water continuously for 7 to 14 days at 1.67 grams of trichlorfon and 7.7 milligrams of atropine per liter.

(3) Prepare fresh solution every 3 days. Do not use simultaneously with other drugs, insecticides, pesticides, or chemicals having cholinesterase activity, nor within 7 days before or after treatment with any other cholinesterase inhibitor.

(4) Restricted to use by or on the order of a licensed veterinarian.

§ 520.2520c Trichlorfon oral liquid.

(a) **Chemical name.** Dimethyl(2,2,2-trichloro-1-hydroxyethyl) phosphonate.

(b) **Sponsor.** See No. 000859 in § 510.600(c) of this chapter.

(c) **Specifications.** Each fluid ounce of the drug contains 3.64 grams of trichlorfon.

(d) **Conditions of use.** (1) The drug is used for removal and control of bots (*Gastrophilus spp.*), ascarids (*Parascaris equorum*), and pinworms (*Oxyuris equi*) in horses and ponies.

(2) Administer by stomach tube at the rate of ½-fluid ounce of trichlorfon oral liquid (1.82 grams trichlorfon) per 100 pounds body weight. Do not fast animals prior to treatment.

(3) Do not treat colts under 4 months of age, mares in the last month of pregnancy, or animals other than horses or ponies. Horses severely debilitated, suffering from diarrhea or severe constipation, infectious disease, toxemia, or colic should not be treated until such conditions are corrected with proper therapy.

(4) Occasional slight transient diarrhea and/or colic may occur soon after administering the drug. Fasting prior to the administration of the drug will increase the likelihood of these side effects occurring in the animals.

(5) Not for use in horses intended for food.

(6) This drug is a cholinesterase inhibitor. Do not use this product on animals simultaneously with, or within 10 days before or after treatment with or exposure to, cholinesterase-inhibiting drugs, pesticides, or chemicals.

(7) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 45164, Oct. 1, 1975]

§ 520.2520d

§ 520.2520d Trichlorfon paste.

(a) *Specifications.* The drug is a paste containing 40-percent trichlorfon. It is packaged in dispensing syringes containing 40 grams of paste (16 grams of trichlorfon).

(b) *Sponsor.* See No. 000859 in § 510.600(c) of this chapter.

(c) *Special considerations.* Trichlorfon is a cholinesterase inhibitor. Do not use this product simultaneously with, or within a few days before or after treatment with or exposure to, cholinesterase-inhibiting drugs, pesticides, or chemicals. Do not administer in conjunction with, or within 1 week of administration of, succinylcholine chloride, phenothiazine-derived tranquilizers, or anesthetics.

(d) *Conditions of use—(1) Amount.* 16 milligrams of trichlorfon per pound of body weight (1.6 grams per 100 pounds).

(2) *Indications for use.* For the control and/or treatment of mouth and stomach stages of bots (*Gastrophilus intestinalis*) and (*Gastrophilus nasalis*), mature ascarids (*Parascaris equorum*), and adult pinworms (*Oxyuris equi*) in horses and foals.

(3) *Limitations.* Administer directly from the syringe on the back of the horse's tongue. Do not administer on an empty stomach. Not for use in horses intended for food. Re-treatment may be necessary for horses maintained on premises where reinfections are likely to occur. For most effective results, re-treat horses in 4 to 8 weeks or as recommended by a veterinarian. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

[43 FR 39084, Sept. 1, 1978]

§ 520.2520e Trichlorfon boluses.

(a) *Specifications.* Each bolus contains either 7.3, 10.9, 14.6, or 18.2 g of trichlorfon.

(b) *Sponsor.* See 000856 in § 510.600(c) of this chapter.

(c) *Special considerations.* Trichlorfon is a cholinesterase inhibitor. Do not use this product on animals simultaneously with, or within 2 weeks, before or after treatment with or exposure to, neuromuscular depolarizing agents (i.e., succinylcholine) or to cho-

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linesterase-inhibiting drugs, pesticides, or chemicals.

(d) *NAS/NRC status.* Use of this drug has been NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter.

(e) *Conditions of use—(1) Amount.* 18.2 milligrams per pound of body weight, except for strongyles use 36.4 milligrams per pound of body weight.

(2) *Indications for use.* For horses for removal of bots (*Gastrophilus nasalis*, *Gastrophilus intestinalis*), large strongyles (*Strongylus vulgaris*), small strongyles, large roundworms (ascarids, *Parascaris equorum*), and pinworms (*Oxyuris equi*).

(3) *Limitations.* Do not fast horses before or after treatment. Treatment of mares in late pregnancy is not recommended. Surgery or any severe stress should be avoided for at least 2 weeks before or after treatment. Do not administer to sick, toxic, or debilitated horses. Not to be used in horses intended for use as food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[45 FR 48127, July 18, 1980]

§ 520.2520f Trichlorfon granules.

(a) *Specifications.* Each package contains either 18.2 or 36.4 g of trichlorfon.

(b) *Sponsor.* See 000856 in § 510.600(c) of this chapter.

(c) *Special considerations.* Trichlorfon is a cholinesterase inhibitor. Do not use this product on animals simultaneously with, or within 2 weeks before or after treatment with or exposure to neuromuscular depolarizing agents (i.e., succinylcholine) or to cholinesterase-inhibiting drugs, pesticides, or chemicals.

(d) *NAS/NRC status.* Use of this drug has been NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter.

(e) *Conditions of use—(1) Amount.* 18.2 milligrams per pound of body weight.

(2) *Indications for use.* For horses for removal of bots (*Gastrophilus na-*

salis, *Gastrophilus intestinalis*), large roundworms (ascarids, *Parascaris equorum*), and pinworms (*Oxyuris equi*).

(3) *Limitations*. Do not fast horses before or after treatment. Treatment of mares in late pregnancy is not recommended. Surgery or any severe stress should be avoided for at least 2 weeks before or after treatment. Do not administer to sick, toxic, or debilitated horses. Not to be used in horses intended for use as food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[45 FR 48128, July 18, 1980]

§ 520.2520g Trichlorfon, phenothiazine, and piperazine dihydrochloride powder.

(a) *Specifications*. Each 54.10 grams (1.91 ounces) of water dispersible powder contains 9.10 grams of trichlorfon, 6.25 grams of phenothiazine, and the equivalent of 20.0 grams of piperazine base (as piperazine dihydrochloride).

(b) *Sponsor*. See No. 000856 in § 510.600(c) of this chapter.

(c) *Special considerations*. Labeling shall bear the following statements: The drug is a cholinesterase inhibitor. Do not use this product in horses simultaneously with, or within 2 weeks before or after treatment with, or exposure to, neuromuscular depolarizing agents (e.g., succinylcholine) or to cholinesterase-inhibiting drugs, pesticides, or chemicals.

(d) *Conditions of use—(1) Amount*. 18.2 milligrams of trichlorfon, 12.5 milligrams of phenothiazine, and 40.0 milligrams of piperazine base per pound of body weight.

(2) *Indications for use*. For horses for removal of bots (*Gastrophilus nasalis*, *Gastrophilus intestinalis*), large strongyles (*Strongylus vulgaris*), small strongyles, large roundworms (ascarids, *Parascaris equorum*), and pinworms (*Oxyuris equi*).

(3) *Limitations*. Mix powder and vial contents together in warm water to form suspension. Administer by stomach tube. Do not fast horses before or after treatment. Treatment of mares in late pregnancy is not recommended. Surgery or any severe stress should be avoided for at least 2 weeks before or

after treatment. Do not administer to sick, toxic, or debilitated horses. Not to be used in horses intended for use as food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[48 FR 2757, Jan. 21, 1983]

§ 520.2520h Trichlorofon and phenothiazine powder.

(a) *Sponsor*. See No. 011531 in § 510.600(c) of this chapter.

(b) *Special considerations*. This drug is a cholinesterase inhibitor. Do not use any drug, insecticide, pesticide, or chemical having cholinesterase-inhibiting activity simultaneously or for a few days before or after treatment.

(c) *Conditions of use—(1)—Amount*.

(i) One 3-ounce package containing 7.477 percent trichlorofon and 17.638 percent phenothiazine for horses of 300 to 400 pounds body weight.

(ii) One 3-ounce package containing 11.205 percent trichlorofon and 23.517 percent phenothiazine for horses of 500 to 700 pounds body weight.

(iii) One 3-ounce package containing 16.803 percent trichlorofon and 29.396 percent phenothiazine for horses of 800 to 1,000 pounds body weight.

(2) *Indications for use*. For horses for the control and removal of bots (*Gastrophilus* spp.), large strongyles (*Strongylus vulgaris*), and small strongyle species.

(3) *Limitations*. Mix entire contents of package with morning feed. Remove and destroy any medicated feed not consumed within 12 hours. Do not retreat within 30 days. Do not treat pregnant mares within 30 days prior to foaling. Do not treat horses to be used for food. Do not treat sick or emaciated horses. Consult your veterinarian for assistance in diagnosis, treatment, and control of parasitism.

[49 FR 7364, Feb. 29, 1984]

§ 520.2582 Triflupromazine hydrochloride tablets.

(a) *Specifications*. Each tablet contains either 10 milligrams or 25 milligrams of triflupromazine hydrochloride.

(b) *Sponsor*. See No. 053501 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used in dogs and cats to relieve anxiety and to help control psychomotor overactivity as well as to increase the tolerance of animals to pain and pruritus. The drug is indicated in various office and clinical procedures which require the aid of a tranquilizer, anesthetic, or preanesthetic.¹

(2) The drug is administered orally to dogs and cats at a dosage level of 1 to 2 milligrams per pound of body weight daily; an initial dosage at the 2-milligram level is suggested followed by daily doses at the 1-milligram level. Frequently, the drug may be withdrawn after 4 to 5 days, with drug effect continuing after withdrawal.¹

(3) Do not use in conjunction with organophosphates and/or procaine hydrochloride, because phenothiazines may potentiate the toxicity of organophosphates and the activity of procaine hydrochloride.¹

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

[40 FR 13838, Mar. 27, 1975, as amended at 50 FR 41489, Oct. 11, 1985]

§ 520.2604 Trimeprazine tartrate and prednisolone tablets.

(a) *Specifications.* Each tablet contains: trimeprazine tartrate, 5 milligrams; and prednisolone, 2 milligrams.

(b) *Sponsor.* See No. 011519 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is administered orally to dogs for the relief of itching regardless of cause; reduction of inflammation commonly associated with most skin disorders of dogs such as eczema, caused by internal disorders, otitis, and dermatitis, allergic, parasitic, pustular and nonspecific. It is also used in dogs as adjunctive therapy in various cough conditions including treatment of "kennel cough" or tracheobronchitis, bronchitis including allergic bronchitis, in tonsillitis, acute upper respiratory infections and coughs of nonspecific origin. The product may also be administered to dogs suffering from acute or chronic bacterial infections, provided the infection is controlled by appropriate antibiotic or chemotherapeutic agents.¹

(2) The drug is administered orally at an initial dosage level of ½ tablet twice daily to dogs weighing up to 10 pounds, one tablet twice daily to dogs weighing 11 to 20 pounds, two tablets twice daily to dogs weighing 21 to 40 pounds, and three tablets twice daily to dogs weighing over 40 pounds. After 4 days, the dosage is reduced to approximately ½ the initial dosage or to an amount just sufficient to maintain remission of symptoms. Dosages in individual cases may vary and should be adjusted until proper response is obtained.¹

(3) Do not use the drug in cases of viral infections involving corneal ulceration or dendritic ulceration of the cornea.¹

(4) Clinical and experimental data have demonstrated that corticosteroids administered orally or parenterally to animals may induce the first stage of parturition when administered during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis.¹

(5) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

§ 520.2605 Trimeprazine tartrate and prednisolone capsules.

(a) *Specifications.* Each capsule contains 3.75 milligrams of trimeprazine in sustained released form (as the tartrate) and 1 milligram of prednisolone (capsule no. 1) or 7.5 milligrams of trimeprazine in sustained release form (as the tartrate) and 2 milligrams of prednisolone (capsule no. 2).

(b) *Sponsor.* See 011519 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* Administer either capsule orally once daily to dogs as follows:

¹ These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

Animal weight (pounds)	Number of capsules per dose	
	Capsule No. 1	Capsule No. 2
Up to 10.....	1	
11 to 20.....	2	1
21 to 40.....	4	2
Over 40.....	6	3

(2) *Indications for use.* For the relief of itching regardless of cause, reduction of inflammation commonly associated with most skin disorders of dogs such as eczema caused by internal disorders, otitis, and dermatitis (allergic, parasitic, pustular, and nonspecific). It is also used in dogs as adjunctive therapy in various cough conditions including treatment of "kennel cough" or tracheobronchitis, bronchitis including allergic bronchitis, tonsillitis, acute upper respiratory infections, and coughs of nonspecific origin. The product may also be administered to dogs suffering from acute or chronic bacterial infections, provided the infection is controlled by appropriate antibiotic or chemotherapeutic agents.

(3) *Limitations.* After 4 days, reduce dosage to one-half the initial dose or to an amount sufficient to maintain remission of symptoms. Dosages in individual cases may vary and should be adjusted until proper response is obtained. Do not use the drug in cases of viral infections involving corneal ulceration or dendritic ulceration of the cornea. Clinical and experimental data have demonstrated that corticosteroids administered orally or parenterally to animals may induce the first stage of parturition when administered during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[48 FR 19367, Apr. 29, 1983]

§ 520.2610 Trimethoprim and sulfadiazine tablets.

(a) *Specifications.* Each tablet contains 30 milligrams (5 milligrams of trimethoprim and 25 milligrams of sulfadiazine), 120 milligrams (20 milligrams of trimethoprim and 100 milli-

grams of sulfadiazine), 480 milligrams (80 milligrams of trimethoprim and 400 milligrams of sulfadiazine) or 960 milligrams (160 milligrams of trimethoprim and 800 milligrams of sulfadiazine).

(b) *Sponsor.* See Nos. 017220 and 000033 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used in dogs where systemic antibacterial action against sensitive organisms is required, either alone or as an adjunct to surgery or debridement with associated infection. The drug is indicated where control of bacterial infection is required during the treatment of acute urinary tract infections, acute bacterial complications of distemper, acute respiratory tract infections, acute alimentary tract infections, wound infections, and abscesses.

(2) The drug is given orally at 30 milligrams per kilogram of body weight per day (14 milligrams per pound per day), or as follows:

Animal body weight (pounds)	Number of tablets
30 MG TABLETS	
2.2.....	1
4.4.....	2
5.6.....	3
8.8.....	4
120 MG TABLETS	
Up to 9.....	1
10 to 19.....	2
20 to 29.....	3
30 to 40.....	4
480 MG TABLETS	
30 to 40.....	1
40 to 60.....	1½
60 to 80.....	2
80 to 110.....	3
Over 110.....	4

(3) The drug is given once daily. Alternatively, especially in severe infections, the initial dose may be followed by one-half the recommended daily dose every 12 hours. If no improvement is seen in 3 days, discontinue therapy and reevaluate diagnosis.

(4) Administer for 2 to 3 days after symptoms have subsided. Do not treat for more than 14 consecutive days.

(5) During long term treatment, periodic platelet counts and white and

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red blood cell counts are recommended.

(6) The drug should not be used in patients showing marked liver parenchymal damage or blood dyscrasia, nor in those with a history of sulfonamide sensitivity.

(7) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[41 FR 3853, Jan. 27, 1976, as amended at 44 FR 32214, June 5, 1979; 46 FR 23231, Apr. 24, 1981; 47 FR 36814, Aug. 24, 1982; 50 FR 9800, Mar. 12, 1985; 50 FR 11852, Mar. 26, 1985]

§ 520.2611 Trimethoprim and sulfadiazine oral paste.

(a) *Specifications.* Each gram of oral paste contains 400 milligrams (67 milligrams of trimethoprim and 333 milligrams of sulfadiazine).

(b) *Sponsor.* See No. 000033 in § 510.600(c) of this chapter for product to be dosed at 5 grams per 150 pounds of body weight per day. See No. 017220 in § 510.600(c) of this chapter for product to be dosed at 3.75 grams per 110 pounds of body weight per day.

(c) *Conditions of use.*—(1) *Dosage.* (i) 5 grams (335 milligrams of trimethoprim and 1,665 milligrams of sulfadiazine) per 150 pounds (68 kilograms) of body weight per day. (ii) 3.75 grams (250 milligrams of trimethoprim and 1,250 milligrams of sulfadiazine) per 110 pounds (50 kilograms) of body weight per day.

(2) *Indications for use.* For horses where systemic anti-bacterial action against sensitive organisms is required during treatment of acute strangles, respiratory infections, acute urogenital infections, and wound infections and abscesses.

(3) *Limitations.* Administer orally, once a day, as a single dose for 5 to 7 days; daily dose may also be halved and given morning and evening; for acute infection therapy continue treatment 2 to 3 days after clinical signs have subsided; if no improvement of acute infections is seen in 3 to 5 days, reevaluate diagnosis; a complete blood count should be done periodically for prolonged use; not for use in horses intended for food; Federal law restricts this drug to use by or on the order of a licensed veterinarian.

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[48 FR 34469, July 29, 1983, as amended at 49 FR 28714, June 29, 1984; 53 FR 11063, Apr. 5, 1988]

§ 520.2612 Trimethoprim and sulfadiazine oral suspension.

(a) *Specifications.* Each milliliter of oral suspension contains 60 milligrams of drug (10 milligrams of trimethoprim and 50 milligrams of sulfadiazine).

(b) *Sponsor.* See No. 017220 in § 510.600 of this chapter.

(c) *Conditions of use: Dogs.*—(1) *Dosage.* 1 milliliter (10 milligrams of trimethoprim and 50 milligrams of sulfadiazine) per 5 pounds of body weight.

(2) *Indications for use.* The drug is used in dogs where systemic antibacterial action against sensitive organisms is required, either alone or as an adjunct to surgery or debridement with associated infection. The drug is indicated where control of bacterial infection is required during the treatment of acute urinary tract infections, acute bacterial complications of distemper, acute respiratory tract infections, acute alimentary tract infections, wound infections, and abscesses.

(3) *Limitations.* For oral use only. Administer the recommended dose once daily or one-half the recommended daily dose every 12 hours. Administer for 2 to 3 days after symptoms have subsided. If no improvement is seen in 3 days, discontinue therapy and reevaluate diagnosis. Do not treat for more than 14 consecutive days. During long-term treatment, a complete blood count is recommended. The drug should not be used in patients showing marked liver parenchymal damage or blood dyscrasia, nor in those with a history of sulfonamide sensitivity. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[50 FR 19168, May 7, 1985]

§ 520.2640 Tylosin.

(a) *Specifications.* Tylosin is the antibiotic substance produced by growth of *Streptomyces fradiae* or the same antibiotic substance produced by any other means. Tylosin, present as the tartrate salt, conforms to the appro-

appropriate antibiotic standard. Tylosin contains at least 95 percent tylosin as a combination of tylosin A, tylosin B, tylosin C, and tylosin D of which at least 80 percent is tylosin A as determined by a method entitled "Determination of Factor Content in Tylosin by High Performance Liquid Chromatography," which is incorporated by reference. Copies are available from the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857, or available for inspection at the Office of the Federal Register, 1100 L St. NW., Washington, DC 20408.

(b) *Sponsor.* See No. 000986 in § 510.600(c) of this chapter.

(c) *Special considerations.* The quantities of antibiotic in paragraph (e) of this section refer to the activity of the appropriate standard.

(d) *Related tolerances.* See § 556.740 of this chapter.

(e) *Conditions of use.* It is used in drinking water of animals as follows:

(1) *Chickens*—(i) *Amount.* 2 grams per gallon.

(ii) *Indications for use.* Aid in the treatment of chronic respiratory disease (CRD) caused by *Mycoplasma gallisepticum* sensitive to tylosin in broiler and replacement chickens. For the control of chronic respiratory disease (CRD) caused by *Mycoplasma gallisepticum* sensitive to tylosin at time of vaccination or other stress in chickens. For the control of chronic respiratory disease (CRD) caused by *Mycoplasma synoviae* sensitive to tylosin in broiler chickens.

(iii) *Limitations.* Do not use in layers producing eggs for human consumption; administer from 1 to 5 days as sole source of drinking water; treated chickens should consume enough medicated drinking water to provide 50 milligrams of tylosin per pound of body weight per day; prepare a fresh solution every 3 days; do not administer within 24 hours of slaughter; as tylosin tartrate.

(2) *Turkeys*—(i) *Amount.* 2 grams per gallon.

(ii) *Indications for use.* Maintaining weight gains and feed efficiency in the presence of infectious sinusitis caused

by *Mycoplasma gallisepticum* sensitive to tylosin.

(iii) *Limitations.* Do not use in layers producing eggs for human consumption; administer from 2 to 5 days as sole source of drinking water; treated turkeys should consume enough medicated drinking water to provide 60 milligrams of tylosin per pound of body weight per day; prepare a fresh solution every 3 days; when sinus swelling is present, inject the sinus with tylosin injectable simultaneously with the drinking water treatment; do not administer within 5 days of slaughter; as tylosin tartrate.

(3) *Swine*—(i) *Amount.* 0.25 gram per gallon.

(ii) *Indications for use.* For the control and treatment of swine dysentery (bloody scours) caused by pathogens sensitive to tylosin.

(iii) *Limitations.* As only source of drinking water for 3 to 10 days, depending on the severity of the condition being treated; mix fresh solution daily; present as tylosin base; medication must be withheld from animals 48 hours prior to slaughter.

[40 FR 13838, Mar. 27, 1975, as amended at 50 FR 49841, Dec. 5, 1985]

PART 522—IMPLANTATION OR INJECTABLE DOSAGE FORM NEW ANIMAL DRUGS NOT SUBJECT TO CERTIFICATION

Sec.

- 522.23 Acepromazine maleate injection.
- 522.44 Sterile sodium acetazolamide.
- 522.46 Alfaprostol.
- 522.56 Amikacin sulfate injection.
- 522.62 Aminopentamide hydrogen sulfate injection.
- 522.82 Aminopropazine fumarate sterile solution injection.
- 522.144 Arsenamide sodium aqueous injection.
- 522.150 Azaperone injection.
- 522.161 Betamethasone acetate and betamethasone disodium phosphate aqueous suspension.
- 522.163 Betamethasone dipropionate and betamethasone sodium phosphate aqueous suspension.
- 522.204 Boldenone undecylenate injection.
- 522.234 Butamisol hydrochloride.
- 522.246 Butorphanol tartrate injection.

Sec.
 522.281 Calcium disodium edetate injection.
 522.311 Carfentanil citrate injection.
 522.313 Ceftriaxone sterile powder for injection.
 522.380 Chloral hydrate, pentobarbital, and magnesium sulfate sterile aqueous solution.
 522.443 Chlorpromazine hydrochloride injection.
 522.460 Cloprostenol sodium.
 522.480 Repository corticotropin injection.
 522.518 Cupric glycinate injection.
 522.540 Dexamethasone injection.
 522.542 Dexamethasone-21-isonicotinate suspension.
 522.563 Diatrizoate meglumine and diatrizoate sodium injection.
 522.690 Dinoprost tromethamine sterile solution.
 522.723 Diprenorphine hydrochloride injection.
 522.740 Disoprenolol sodium injection.
 522.775 Doxapram hydrochloride injection.
 522.784 Doxylamine succinate injection.
 522.800 Droperidol and fentanyl citrate injection.
 522.820 Erythromycin injection.
 522.840 Estradiol.
 522.842 Estradiol benzoate and testosterone propionate in combination.
 522.850 Estradiol valerate and norgestomet in combination.
 522.863 Ethylisobutrazine hydrochloride injection.
 522.883 Etorphine hydrochloride injection.
 522.900 Euthanasia solution.
 522.914 Fenpropalene solution.
 522.940 Colloidal ferric oxide injection.
 522.960 Flumethasone implantation or injectable dosage forms.
 522.960a Flumethasone suspension.
 522.960b Flumethasone acetate injection.
 522.960c Flumethasone solution.
 522.970 Flunixin meglumine solution.
 522.995 Fluprostenoil sodium injection.
 522.1010 Purosemide injection.
 522.1020 Gelatin solution.
 522.1044 Gentamicin sulfate injection.
 522.1060 Glyceryl guaiacolate implantation or injectable dosage forms. [Reserved]
 522.1060a Glyceryl guaiacolate sterile powder.
 522.1060b Glyceryl guaiacolate injection.
 522.1066 Glycopyrrrolate injection.
 522.1078 Gonadorelin diacetate tetrahydrate injection.
 522.1081 Chorionic gonadotropin for injection; chorionic gonadotropin suspension.
 522.1085 Guaifenesin sterile powder.
 522.1145 Hyaluronic acid sodium injection.
 522.1150 Hydrochlorothiazide injection.
 522.1155 Imidocarb dipropionate sterile powder.
 522.1182 Iron dextran complex injection.

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 522.1183 Iron hydrogenated dextran injection.
 522.1192 Ivermectin injection.
 522.1204 Kanamycin sulfate injection.
 522.1222 Ketamine hydrochloride injectable dosage forms.
 522.1222a Ketamine hydrochloride injection.
 522.1222b Ketamine hydrochloride with promazine hydrochloride and aminopentamide hydrogen sulfate injection.
 522.1228 Lactic acid.
 522.1235 Lenperone hydrochloride injection.
 522.1244 Levamisole phosphate injection.
 522.1258 Lidocaine injection with epinephrine.
 522.1260 Lincomycin injection.
 522.1372 Mepivacaine hydrochloride injection.
 522.1380 Methocarbamol injection.
 522.1410 Sterile methylprednisolone acetate suspension.
 522.1452 Nalorphine hydrochloride injection.
 522.1462 Naloxone hydrochloride injection.
 522.1468 Naproxen for injection.
 522.1484 Neomycin sulfate sterile solution.
 522.1503 Neostigmine methylsulfate injection.
 522.1563 Nitrofurantoin sodium injection.
 522.1610 Oleate sodium solution.
 522.1620 Orgotein for injection.
 522.1642 Oxymorphone hydrochloride injection.
 522.1660 Oxytetracycline injection.
 522.1662 Oxytetracycline hydrochloride implantation or injectable dosage forms.
 522.1662a Oxytetracycline hydrochloride injection.
 522.1662b Oxytetracycline hydrochloride with lidocaine injection.
 522.1680 Oxytocin injection.
 522.1698 Pentazocine lactate injection.
 522.1704 Sodium pentobarbital injection.
 522.1720 Phenylbutazone injection.
 522.1800 Piperacetazine injection.
 522.1820 Pituitary luteinizing hormone for injection.
 522.1822 Follicle stimulating hormone-pituitary for injection.
 522.1850 Polysulfated glycosaminoglycan.
 522.1862 Sterile pralidoxime chloride.
 522.1870 Praziquantel injectable solution.
 522.1880 Sterile prednisolone suspension.
 522.1881 Sterile prednisolone acetate aqueous suspension.
 522.1883 Prednisolone sodium phosphate injection, sterile.
 522.1884 Prednisolone sodium succinate injection.
 522.1885 Prednisolone tertiary butylacetate suspension.
 522.1890 Sterile prednisone suspension.

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- 522.1920 Prochlorperazine, isopropamide for injection.
- 522.1940 Progesterone and estradiol benzoate in combination.
- 522.1962 Promazine hydrochloride injection.
- 522.2002 Propiopromazine hydrochloride injection.
- 522.2012 Prostalene solution.
- 522.2022 Protokylol hydrochloride injection.
- 522.2063 Pyrilamine maleate injection.
- 522.2100 Selenium, vitamin E injection.
- 522.2120 Spectinomycin injection.
- 522.2150 Stanozolol sterile suspension.
- 522.2200 Sulfachlorpyridazine.
- 522.2220 Sulfadimethoxine injection.
- 522.2240 Sulfathoxypyridazine.
- 522.2260 Sulfamethazine injectable solution.
- 522.2340 Sulfomycin.
- 522.2404 Thalbarbitone sodium for injection.
- 522.2424 Sodium thiamylal for injection.
- 522.2444 Sodium thiopental implantation or injectable dosage forms.
- 522.2444a Sodium thiopental for injection.
- 522.2444b Sodium thiopental, sodium pentobarbital for injection.
- 522.2470 Tiletamine hydrochloride and zolazepam hydrochloride for injection.
- 522.2476 Trenbolone acetate.
- 522.2480 Triamcinolone injection.
- 522.2483 Sterile triamcinolone acetate suspension.
- 522.2582 Triflupromazine hydrochloride injection.
- 522.2610 Trimethoprim and sulfadiazine sterile suspension.
- 522.2615 Tripelennamine hydrochloride injection.
- 522.2640 Tylosin injectable dosage forms.
- 522.2640a Tylosin injection.
- 522.2640b Tylosin tartrate for injection.
- 522.2662 Xylazine hydrochloride injection.
- 522.2680 Zeranol.

AUTHORITY: Sec. 512(l), 82 Stat. 347 (21 U.S.C. 360b(l)); 21 CFR 5.10 and 5.83.

SOURCE: 40 FR 13858, Mar. 27, 1975, unless otherwise noted.

§ 522.23 Acepromazine maleate injection.

(a) *Specifications.* Each milliliter of sterile aqueous solution contains 10 milligrams of acepromazine maleate.

(b) *Conditions of use.* See No. 000856 in § 510.600(c) of this chapter for use in dogs, cats, and horses as follows:

(1) *Indications for use.* It is used in dogs, cats, and horses as a tranquilizer.

(2) *Amount.* Dogs: 0.25 to 0.5 milligram per pound of body weight; Cats: 0.5 to 1.0 milligram per pound of body

weight; Horses: 2.0 to 4.0 milligrams per 100 pounds of body weight.

(c) *Conditions of use.* See No. 054273 in § 510.600(c) of this chapter for use in dogs as follows:

(1) *Indications for use.* It is used in dogs as an aid in tranquilization and as a preanesthetic agent.

(2) *Amount.* Dogs: 0.25 to 0.5 milligram per pound of body weight.

(3) *Limitations.* The drug is administered intravenously, intramuscularly or subcutaneously with the dosage individualized depending upon the degree of tranquilization required. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[46 FR 43831, Sept. 1, 1981, as amended at 53 FR 40727, Oct. 18, 1988]

§ 522.44 Sterile sodium acetazolamide.

(a) *Specifications.* Sterile sodium acetazolamide contains acetazolamide sodium complying with United States Pharmacopeia as a sterile powder with directions for reconstituting the product with sterile distilled water to furnish a product having a concentration of 100 milligrams acetazolamide activity per milliliter.

(b) *Sponsor.* See No. 010042 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is used as an aid in the treatment of dogs with mild congestive heart failure and for rapid reduction of intraocular pressure.¹

(2) It is administered intramuscularly or intraperitoneally to dogs at a level of 5 to 15 milligrams per pound of body weight daily preferably administered in two or more divided doses.¹

(3) For use only by or on the order of a licensed veterinarian.¹

§ 522.46 Alfaprostol.

(a) *Specifications.* Each milliliter of sterile solution contains 1 milligram of alfaprostol.

¹ These conditions are N.A.S./N.R.C. reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

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(b) *Sponsor.* No. 055882 in § 510.600(c) of this chapter.

(c) *Conditions of use.* It is used in horses as follows:

(1) *Amount.* For average mature mares, 6.0 micrograms per kilogram of body weight.

(2) *Indications for use.* To cause luteolysis in mares with active corpora lutea.

(3) *Limitations.* For intramuscular or subcutaneous use as a single injection. Not for horses intended for food. Alfaprostol is readily absorbed through the skin and can cause abortion and/or bronchial spasms. Women of childbearing age, asthmatics, and persons with bronchial and other respiratory problems should exercise extreme caution when handling this product. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[48 FR 43300, Sept. 23, 1983, as amended at 53 FR 40057, Oct. 13, 1988]

§ 522.56 Amikacin sulfate injection.

(a) *Specifications.* Each milliliter of sterile aqueous solution contains 50 milligrams of amikacin (as the sulfate).

(b) *Sponsor.* See 000856 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* 5 milligrams per pound of body weight twice daily.

(2) *Indications for use.* The drug is used in dogs for treatment of genitourinary tract infections (cystitis) caused by susceptible strains of *Escherichia coli* and *Proteus* spp. and skin and soft tissue infections caused by susceptible strains of *Pseudomonas* spp. and *E. coli*.

(3) *Limitations.* The drug is administered intramuscularly or subcutaneously. Treat dogs with skin and soft tissue infections for a minimum of 7 days and those with genitourinary infections for 7 to 21 days or until culture is negative and asymptomatic. If no response is observed after 3 days of treatment, therapy should be discontinued and the case reevaluated. Maximum duration of therapy should not exceed 30 days. Systemic aminoglycoside therapy is contraindicated in dogs with seriously impaired renal function. Not for use in breeding dogs as repro-

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ductive studies have not been conducted. Use with extreme caution in dogs in which hearing acuity is required for functioning. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[52 FR 11816, Apr. 13, 1987; 52 FR 15412, Apr. 28, 1987, as amended at 53 FR 27851, July 25, 1988]

§ 522.62 Aminopentamide hydrogen sulfate injection.

(a) *Chemical name.* 4-(Dimethylamino)-2,2-diphenylvaleramide hydrogen sulfate.

(b) *Specifications.* It is sterile and each milliliter of aqueous solution contains 0.5 milligram of the drug.

(c) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(d) *Conditions of use.* (1) It is intended for use in dogs and cats only for the treatment of vomiting and/or diarrhea, nausea, acute abdominal visceral spasm, pylorospasm, or hypertrophic gastritis.

NOTE: Not for use in animals with glaucoma because of the occurrence of mydriasis.

(2) Dosage is administered by subcutaneous or intramuscular injection every 8 to 12 hours, as follows:

Weight of animal in pounds	Dosage in milligrams
Up to 10	0.1
11 to 20	0.2
21 to 50	0.3
51 to 100	0.4
Over 100	0.5

Dosage may be gradually increased up to a maximum of five times the suggested dosage. Following parenteral use dosage may be continued by oral administration of tablets.

(3) For use only by or on the order of a licensed veterinarian.

[40 FR 13858, Mar. 27, 1975, as amended at 53 FR 27851, July 25, 1988]

§ 522.82 Aminopropazine fumarate sterile solution injection.

(a) *Specifications.* Each milliliter of aminopropazine fumarate sterile aqueous solution, veterinary, contains aminopropazine fumarate equivalent

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to 25 milligrams of aminopropazine base.

(b) *Sponsor.* See No. 017220 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used for reducing excessive smooth muscle contractions, such as occur in urethral spasms associated with urolithiasis in cats and dogs and in colic spasms in horses.¹

(2) It is administered intramuscularly or intravenously to dogs and cats at a level of 1 to 2 milligrams per pound of body weight. It is administered intramuscularly or intravenously to horses at a level of 0.25 milligrams per pound of body weight. Dosage can be repeated every 12 hours, as indicated.¹

(3) Not for use in animals intended for food purposes.¹

(4) For use only by or on the order of a licensed veterinarian.¹

[40 FR 13858, Mar. 27, 1975, as amended at 46 FR 48642, Oct. 2, 1981]

§ 522.144 Arsenamide sodium aqueous injection.

(a) *Chemical name.* [(p-Carbamoylphenyl) arylene]dithio diacetic acid, sodium salt.

(b) *Specifications.* The drug is a sterile aqueous solution and each milliliter contains 10.0 milligrams of arsenamide sodium.

(c) *Sponsor.* See Nos. 020112 and 050604 in § 510.600(c) of this chapter.

(d) *Conditions of use.* (1) For the treatment and prevention of canine heartworm disease caused by *Dirofilaria immitis*.

(2) It is administered intravenously at 0.1 milliliter per pound of body weight (1.0 milliliter for every 10 pounds) twice a day for 2 days. For dogs in poor condition, particularly those with evidence of reduced liver function, a more conservative dosage schedule of 0.1 milliliter per pound of body weight daily for 15 days is recommended.

(3) Restricted to use only by or on the order of a licensed veterinarian.

¹ These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

[40 FR 13858, Mar. 27, 1975, as amended at 43 FR 27785, June 27, 1978; 45 FR 56798, Aug. 26, 1980]

§ 522.150 Azaperone injection.

(a) *Specifications.* Each milliliter of sterile aqueous solution contains 40 milligrams of azaperone.

(b) *Sponsor.* See No. 011716 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) *Indications for use.* Control of aggressiveness when mixing or regrouping weanling or feeder pigs weighing up to 80 pounds.

(2) *Dosage.* 2.2 milligrams per kilogram (1 milligram per pound).

(3) *Limitations.* Inject by deep intramuscular injection. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[48 FR 48229, Oct. 18, 1983]

§ 522.161 Betamethasone acetate and betamethasone disodium phosphate aqueous suspension.

(a) *Chemical names.* Betamethasone acetate: 9- α -Fluoro-16- β -methylprednisolone-21-acetate (C₂₈H₃₁F O₆). Betamethasone disodium phosphate: 9- α -Fluoro-16- β -methylprednisolone-21-disodium phosphate (C₂₂H₂₉F Na₂O₆P).

(b) *Specifications.* The drug is a sterile aqueous suspension and each cubic centimeter contains: 12 milligrams of betamethasone acetate (equivalent to 10.8 milligrams of betamethasone), 3.9 milligrams of betamethasone disodium phosphate (equivalent to 3 milligrams of betamethasone), 2 milligrams of dibasic sodium phosphate, 5 milligrams of sodium chloride, 0.1 milligram of disodium EDTA, 0.5 milligram of polysorbate 80, 9 milligrams of benzyl alcohol, 5 milligrams of sodium carboxymethylcellulose, 1.8 milligrams of methylparaben, 0.2 milligram of propylparaben, hydrochloric acid and/or sodium hydroxide to adjust pH, and water for injection q.s.

(c) *Sponsor.* See No. 000061 in § 510.600(c) of this chapter.

(d) *Conditions of use.* It is used or intended for use by intra-articular injection of horses for the treatment of various inflammatory joint conditions; for example, acute and traumatic

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lameness involving the carpal and fetlock joints. Administer from 2.5 to 5 cubic centimeters per dose. Dose may be repeated when necessary depending upon the duration of relief obtained. Not for use in horses intended for food. For use only by or on the order of a licensed veterinarian.

[40 FR 13858, Mar. 27, 1975, as amended at 52 FR 7832, Mar. 13, 1987]

§ 522.163 Betamethasone dipropionate and betamethasone sodium phosphate aqueous suspension.

(a) *Specifications.* Betamethasone dipropionate and betamethasone sodium phosphate aqueous suspension is a sterile aqueous suspension. Each milliliter of the suspension contains the equivalent of 5 milligrams of betamethasone as betamethasone dipropionate and 2 milligrams of betamethasone as betamethasone sodium phosphate.

(b) *Sponsor.* See No. 000061 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Dogs.* (i) It is used as an aid in the control of pruritus associated with dermatoses.

(ii) It is administered by intramuscular injection at a dosage of 0.25 to 0.5 milliliter per 20 pounds of body weight, depending on the severity of the condition. Frequency of dosage depends on recurrence of pruritic symptoms. Dosage may be repeated every 3 weeks or when symptoms recur, not to exceed a total of 4 injections.

(2) *Horses.* (i) It is used as an aid in the control of inflammation associated with various arthropathies.

(ii) It is administered aseptically by intraarticular injection at a dosage of 2.5 to 5 milliliters per joint, depending on the severity of the condition and the joint size. Dosage may be repeated upon recurrence of clinical signs. Injection into the joint cavity should be preceded by withdrawal of synovial fluid.

(iii) Not for use in horses intended for food.

(3) *Clinical and experimental data.* It has been demonstrated that corticosteroids administered orally or parenterally to animals may induce the first stage of parturition when administered during the last trimester of pregnancy and may precipitate prema-

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ture parturition followed by dystocia, fetal death, retained placenta, and metritis.

(4) *Restrictions.* Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13858, Mar. 27, 1975, as amended at 41 FR 27316, July 2, 1976; 52 FR 7832, Mar. 13, 1987]

§ 522.204 Boldenone undecylenate injection.

(a) *Specifications.* Each milliliter contains 25 or 50 milligrams of boldenone undecylenate in a sesame oil base.

(b) *Sponsor.* See No. 053501 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is intended for use as an aid in treating debilitated horses following disease or overwork and overexertion when an improvement in weight, hair coat, or general physical condition is desired. The drug is given only as adjunctive therapy to other specific and supportive therapy for diseases, surgical cases, and traumatic injuries. Optimal results can be expected only when good management and feeding practices are followed.

(2) It is administered intramuscularly at a dosage level of 0.5 milligram per pound of body weight. Treatment may be repeated at 3-week intervals.

(3) For use in horses only. Do not administer to horses intended for use as food. The effectiveness of the drug in stallions and pregnant mares has not been established, nor has the drug been shown not to be teratogenic in pregnant mares; therefore, this drug should not be used in stallions and pregnant mares.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13858, Mar. 27, 1975, as amended at 50 FR 41489, Oct. 11, 1985]

§ 522.234 Butamisol hydrochloride.

(a) *Specifications.* The drug contains 11 milligrams of butamisol per milliliter in a solution consisting of 70 percent propylene glycol, 4 percent benzyl alcohol and distilled water.

(b) *Sponsor.* See Nos. 000859 and 043781 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is administered by subcutaneous injection to dogs for the treatment of infections with whipworms (*Trichuris vulpis*), and the hookworm (*Ancylostoma caninum*).

(2) The drug is administered subcutaneously at the rate of 0.1 milliliter per pound of body weight. In problem cases, retreatment for whipworms may be necessary in approximately 3 months. For hookworms, a second injection should be given 21 days after the initial treatment.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[43 FR 15625, Apr. 14, 1978. Redesignated at 43 FR 60883, Dec. 29, 1978, and amended at 45 FR 29789, May 6, 1980; 51 FR 19329, May 29, 1986]

§ 522.246 Butorphanol tartrate injection.

(a) *Specifications.* Each milliliter of aqueous solution contains either 0.5 or 10 milligrams of butorphanol (as butorphanol tartrate).

(b) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Dogs—(i) Amount.* 0.025 milligram of butorphanol base activity per pound of body weight (equivalent to 0.5 milliliter per 10 pounds), using 0.5 milligram per milliliter solution.

(ii) *Indications for use.* For the relief of chronic nonproductive cough associated with tracheo-bronchitis, tracheitis, tonsillitis, laryngitis, and pharyngitis associated with inflammatory conditions of the upper respiratory tract.

(iii) *Limitations.* For subcutaneous injection in dogs only. Repeat at intervals of 6 to 12 hours as required. If necessary, increase dose to maximum of 0.05 milligram per pound of body weight. Treatment should not normally be required for longer than 7 days. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(2) *Horses—(i) Amount.* 0.05 milligram of butorphanol base activity per pound of body weight (0.1 milligram/kilogram) using 10 milligrams per milliliter solution.

(ii) *Indications for use.* For the relief of pain associated with colic and post-

partum pain in adult horses and yearlings.

(iii) *Limitations.* For intravenous use in horses only. Dose may be repeated within 3 to 4 hours. Treatment should not exceed 48 hours. Not for use in horses intended for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[45 FR 29276, May 2, 1980, as amended at 50 FR 24508, June 11, 1985; 53 FR 27851, July 25, 1988]

§ 522.281 Calcium disodium edetate injection.

(a) *Specifications.* Calcium disodium edetate injection contains 6.6-percent calcium disodium edetate in purified water.

(b) *Sponsor.* See No. 000859 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is used as an aid in the treatment of acute lead poisoning in horses.¹

(2) It is administered by slow intravenous injection at the rate of 1 milliliter per 2 pounds of body weight daily. It is best administered in divided doses 2 to 3 times daily and continued for 3 to 5 days. If additional treatment is indicated, a 2-day rest period is recommended which may be followed by another 3- to 5-day period of therapy.¹

(3) Do not use in horses intended for food purposes.¹

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

[40 FR 13858, Mar. 27, 1975, as amended at 42 FR 65151, Dec. 30, 1977]

§ 522.311 Carfentanil citrate injection.

(a) *Specifications.* Each milliliter of sterile aqueous solution contains 3 milligrams of carfentanil citrate.

(b) *Sponsor.* See No. 053923 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* 5 to 20 micrograms per kilogram (.005 to .020 milligram per kilogram) of body weight.

¹These conditions of use are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter.

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(2) *Indications for use.* For immobilizing free ranging and confined members of the family Cervidae (deer, elk, and moose).

(3) *Limitations.* Inject into large muscle of neck, shoulder, back, or hindquarter. Avoid intrathoracic, intra-abdominal, or subcutaneous injection. To reverse effect, use 7 milligrams of diprenorphine for each milligram of carefentanil citrate, given intravenously or one-half intravenously and one-half intramuscularly or subcutaneously. Do not use in domestic animals intended for food. Do not use 30 days before or during hunting season. Do not use in animals that display clinical signs of severe cardiovascular or respiratory disease. Available data are inadequate to recommend use in pregnant animals. Avoid use during breeding season. Federal law restricts this drug to use by or on the order of a licensed veterinarian. The licensed veterinarian shall be a veterinarian engaged in zoo and exotic animal practice, wildlife management programs, or research.

[53 FR 40057, Oct. 13, 1988]

§ 522.313 Ceftiofur sterile powder for injection.

(a) *Specifications.* Ceftiofur sodium sterile powder for injection is reconstituted to form an aqueous solution containing the equivalent of 50 milligrams ceftiofur per milliliter.

(b) *Sponsor.* See 000009 in § 510.600 of this chapter.

(c) *Related tolerances.* See § 556.113 of this chapter.

(d) *Conditions of use—(1) Cattle—(i) Amount.* 0.5 milligram ceftiofur per pound of body weight intramuscularly.

(ii) *Indications for use.* Treatment of bovine respiratory disease (shipping fever, pneumonia) associated with *Pasteurella hemolytica*, *P. multocida*, and *Haemophilus somnus* in beef and non-lactating dairy cattle.

(iii) *Limitations.* Treatment should be repeated once every 24 hours for 3 days. Treat for an additional 2 days if animals do not show a satisfactory response. Do not use in animals previously found to be hypersensitive to the drug. Use of doses in excess of those indicated may result in illegal

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residues in tissues. Not for use in lactating dairy animals. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(2) [Reserved]

[53 5369, Feb. 24, 1988]

§ 522.380 Chloral hydrate, pentobarbital, and magnesium sulfate sterile aqueous solution.

(a) [Reserved]

(b)(1) *Specifications.* Chloral hydrate, pentobarbital, and magnesium sulfate sterile aqueous solution contains 42.5 milligrams of chloral hydrate, 8.86 milligrams of pentobarbital, and 21.2 milligrams of magnesium sulfate in each milliliter of sterile aqueous solution containing water, 33.8 percent propylene glycol, and 14.25 percent ethyl alcohol.

(2) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) It is used for general anesthesia and as a sedative-relaxant in cattle and horses.

(ii) For intravenous use only. The drug is administered at a dosage level of 20 to 50 milliliters per 100 pounds of body weight for general anesthesia until the desired effect is produced. Cattle usually require a lower dosage on the basis of body weight. When used as a sedative-relaxant, it is administered at a level of one-fourth to one-half of the anesthetic dosage level.

(iii) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13858, Mar. 27, 1975, as amended at 45 FR 16482, Mar. 14, 1980]

§ 522.443 Chlorpromazine hydrochloride injection.

(a) *Specifications.* Chlorpromazine hydrochloride injection contains 25 milligrams of chlorpromazine hydrochloride in each milliliter.

(b) *Sponsor.* See No. 011716 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is administered either intramuscularly or intravenously to dogs and cats as a tranquilizer, potentiator, and antiemetic with a sedating effect.¹

(2) It is administered to dogs and cats intravenously at a dosage level of

25 milligrams per 12.5 to 100 pounds body weight. It is administered intramuscularly at a dosage level of 25 milligrams per 8 pounds to 50 pounds body weight. It is administered one to four times daily depending upon size of dose and the needs of the patient.¹

(3) It is not to be used in conjunction with organophosphates and/or procaine hydrochloride since phenothiazines may potentiate the toxicity of organophosphates and the activity of procaine hydrochloride.¹

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

§ 522.460 Cloprostenol sodium.

(a)(1) *Specifications.* Each milliliter of the aqueous solution contains 263 micrograms of cloprostenol sodium (equivalent to 250 micrograms of cloprostenol) in a sodium citrate, anhydrous citric acid and sodium chloride buffer containing 0.1 percent w/v chlorocresol B.P. as a bactericide.

(2) *Sponsor.* See No. 000859 in § 510.600(c) of this chapter.

(3) *Conditions of use.* For intramuscular use in beef and dairy cattle to induce luteolysis.

(i) *Amount.* 2 milliliters (equivalent to 500 micrograms of cloprostenol).

(ii) *Indications.* (a) For scheduling estrus and ovulation to control the time at which cycling cows or heifers can be bred.

(1) *Single cloprostenol injection.* Treat only animals with a mature corpus luteum. Estrus should occur in 2 to 5 days, and cattle should be inseminated at the usual time relative to the detection of estrus. If estrus is not observed, treated animals may be inseminated either once at 72 hours post injection or twice at 72 and 96 hours post injection.

(2) *Double cloprostenol injection.* Give cattle a second injection 11 days after the first injection. Estrus should occur 2 to 5 days after the second injection, and cattle should be inseminated at the usual time relative to the detection of estrus. If estrus is not observed, treated animals may be inseminated either once at 72 hours post injection or twice at 72 and 96 hours following the second injection.

(b) *Single cloprostenol injection for terminating unwanted pregnancies from mismatings from 1 week after mating until 5 months after conception, or for treating unobserved (non-detected) estrus, mummified fetus, and luteal cysts.*

(c) *Single cloprostenol injection for the treatment of pyometra.*

(iii) Do not administer to pregnant animals where the calf is not to be aborted.

(iv) Women of childbearing age, asthmatics, and persons with bronchial and other respiratory problems should exercise extreme caution when handling this product. Cloprostenol is readily absorbed through the skin and may cause abortion and/or bronchospasms. Accidental spillage on the skin should be washed off immediately with soap and water.

(v) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(b)(1) *Specifications.* Each milliliter of sterile aqueous solution contains 131.5 micrograms of cloprostenol sodium (equivalent to 125 micrograms of cloprostenol).

(2) *Sponsor.* See No. 000859 in § 510.600(c) of this chapter.

(3) *Special considerations.* Labeling shall bear the statements prescribed in paragraphs (a)(3) (iii) and (iv) of this section.

(4) *Conditions of use—(i) Amount.* 3 milliliters (equivalent to 375 micrograms of cloprostenol) intramuscularly per animal as a single dose.

(ii) *Indications for use.* To induce abortion in pregnant feedlot heifers from 1 week after mating until 4½ months of gestation.

(iii) *Limitations.* Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(47 FR 4678, Feb. 2, 1982, as amended at 48 FR 15619, Apr. 12, 1983; 49 FR 5100, Feb. 10, 1984; 49 FR 29957, July 25, 1984]

¹ These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

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§ 522.480 Repository corticotropin injection.

(a)(1) *Specifications.* The drug conforms to repository corticotropin injection U.S.P. It contains 40 or 80 U.S.C. (I.U.) units per cubic centimeter.

(2) *Sponsor.* See No. 037990 in § 510.600(c) of this chapter.

(3) *Special considerations.* The drug should be refrigerated. With prolonged use supplement daily diet with potassium chloride at one gram for small animals and from 5 to 10 grams for large animals.

(4) *Conditions of use.* (i) It is used as an intramuscular or subcutaneous injection in cattle and small animals for stimulation of the adrenal cortex where there is a general deficiency of corticotropin (ACTH). It is also a therapeutic agent for primary bovine ketosis.

(ii) It is administered to cattle initially at 200 to 600 units followed by a dose daily or every other day of 200 to 300 units and to small animals at one unit per pound of body weight to be repeated as indicated.

(iii) For use only by or on the order of a licensed veterinarian.

(b)(1) *Specifications.* The drug conforms to repository corticotropin injection U.S.P. It contains 40 or 80 U.S.P. units per milliliter.

(2) *Sponsor.* See No. 000864 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) For intramuscular injection in dogs as a diagnostic aid to test for adrenal dysfunction. For intramuscular or subcutaneous injection in dogs and cats for stimulation of the adrenal cortex, where there is a general deficiency of ACTH.

(ii) For diagnostic use: Administer at one unit per pound of body weight intramuscularly. For therapeutic use: Administer at one unit per pound of body weight intramuscularly or subcutaneously, initially, to be repeated as indicated.

(iii) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(c) *National Academy of Sciences/National Research Council (NAS/NRC) status.* The therapeutic indication for use has been reviewed by NAS/NRC and found to be effective.

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Applications for this use need not include effectiveness data as specified in § 514.111 of this chapter, but may require bioequivalency and safety information.

[40 FR 13858, Mar. 27, 1985, as amended at 50 FR 40966, Oct. 8, 1985; 53 FR 45760, Nov. 14, 1988]

§ 522.518 Cupric glycinate injection.

(a) *Specifications.* Each milliliter (mL) of sterile aqueous suspension contains 200 milligrams of cupric glycinate (equivalent to 60 milligrams of copper).

(b) *Sponsor.* See 000061 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* 200 milligrams (1 mL) for calves 300 pounds and under; 400 milligrams (2 mL) for calves over 300 pounds and adult cattle.

(2) *Indications for use.* For beef calves and beef cattle for the prevention of copper deficiency, or when labeled for veterinary prescription use, for the prevention and/or treatment of copper deficiency alone or in association with molybdenum toxicity.

(3) *Limitations.* For subcutaneous use only; repeat dose in 3 months in young calves, in 6 months in cattle; discontinue use 30 days before treated animals are slaughtered for food use; Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[46 FR 20159, Apr. 3, 1981, as amended at 52 FR 7832, Mar. 13, 1987]

§ 522.540 Dexamethasone injection.

(a)(1) *Specifications.* The drug is a sterile aqueous solution. Each milliliter contains 2 mg of dexamethasone.

(2) *Sponsor.* See No. 000061 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) The drug is indicated for the treatment of primary bovine ketosis and as an anti-inflammatory agent in dogs, cats, cattle, and horses.¹

(ii) The drug is administered intravenously or intramuscularly and dosage may be repeated if necessary, as follows:¹

- (a) Canine—0.25 to 1 mg.
- (b) Feline—0.125 to 0.5 mg.
- (c) Equine—2.5 to 5 mg.

(d) Bovine—5 to 20 mg depending on the severity of the condition.

(iii) Clinical and experimental data have demonstrated that corticosteroids administered orally or parenterally to animals may induce the first stage of parturition when administered during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis.

(iv) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(b)(1) *Specifications.* The drug is a sterile aqueous solution. Each milliliter contains either 2.0 milligrams of dexamethasone or 4.0 milligrams of dexamethasone sodium phosphate (equivalent to 3.0 milligrams dexamethasone).

(2) *Sponsor.* See number in § 510.600(c) of this chapter as follows:

(i) No. 000864 for use of 2.0 milligrams dexamethasone or 4.0 milligrams dexamethasone sodium phosphate injections.

(ii) No. 000402 for use of 2.0 milligrams dexamethasone or 4.0 milligrams dexamethasone sodium phosphate injections.

(3) *Conditions of use.* (i) The drug is used in dogs for the treatment of inflammatory conditions, as supportive therapy in canine posterior paresis, as supportive therapy before or after surgery to enhance recovery of poor surgical risks, and as supportive therapy in nonspecific dermatosis.¹

(ii) The drug is administered intravenously at 0.25 to 1 milligram initially. The dose may be repeated for 3 to 5 days or until a response is noted. If continued treatment is required, oral therapy may be substituted. When therapy is withdrawn after prolonged use, the daily dose should be reduced gradually over several days.¹

(iii) Clinical and experimental data have demonstrated that corticosteroids administered orally or parenterally to animals may induce the first

stage of parturition when administered during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis.

(iv) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(c)(1) *Specifications.* The drug is a sterile aqueous solution. Each milliliter contains 2.0 milligrams of dexamethasone or 4.0 milligrams of dexamethasone sodium phosphate (equivalent to 3.0 milligrams of dexamethasone).

(2) *Sponsor.* See Nos. 000402 and 000864 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) The drug is used as a rapid adrenal glucocorticoid and/or anti-inflammatory agent in horses.¹

(ii) The drug is administered intravenously at a dosage of 2.5 to 5.0 milligrams. If permanent corticosteroid effect is required, oral therapy may be substituted. When therapy is withdrawn after prolonged use, the daily dose should be reduced gradually over several days.¹

(iii) Clinical and experimental data have demonstrated that corticosteroids administered orally or parenterally to animals may induce the first stage of parturition when administered during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis.

(iv) Not for use in horses intended for food.

(v) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(d)(1) *Specifications.* The drug is a sterile aqueous solution. Each milliliter contains 2.0 milligrams of dexamethasone or 4.0 milligrams of dexamethasone sodium phosphate (equivalent to 3.0 milligrams of dexamethasone).

(2) *Sponsors.* See the following numbers in § 510.600(c) of this chapter:

(i) Nos. 000029, 010271, and 053617 for intravenous or intramuscular use of 2.0 milligrams dexamethasone injection.

(ii) 010719 for intravenous use of 4.0 milligrams dexamethasone sodium

¹ These conditions are NAS/NRC-reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

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phosphate (equivalent to 3.0 milligrams of dexamethasone) injection.

(iii) No. 000069 for intravenous use of 2.0 milligrams dexamethasone injection.

(3) *Conditions of use.* (i) The drug is used as an anti-inflammatory agent in dogs, cats, and horses.

(ii) It is administered intravenously or intramuscularly as follows: dogs—0.25 to 1 milligram; cats—0.125 to 0.5 milligram; horses—2.5 to 5 milligrams.

(iii) Clinical and experimental data have demonstrated that corticosteroids administered orally or by injection to animals may induce the first stage of parturition when administered during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis.

(iv) Not for use in horses intended for food.

(v) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(e)(1) *Specifications.* The drug is a sterile aqueous solution. Each milliliter contains 4.0 milligrams of dexamethasone sodium phosphate (equivalent to 3 milligrams of dexamethasone).

(2) *Sponsors.* See Nos. 010271 and 053617 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) The drug is given for glucocorticoid and anti-inflammatory effect in dogs and horses.

(ii) Administer intravenously as follows: Dogs—0.25 to 1 milligram initially; may be repeated for 3 to 5 days or until response is noted. Horses—2.5 to 5 milligrams. If permanent glucocorticoid effect is required, oral therapy may be substituted. When therapy is to be withdrawn after prolonged use, the daily dose should be reduced gradually over several days.

(iii) Clinical and experimental data have demonstrated that corticosteroids administered orally or by injection may induce the first stage of parturition when administered during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis.

(iv) Do not use in viral infections. Anti-inflammatory action of corticosteroids may mask signs of infections.

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Except when used for emergency therapy, the product is contraindicated in animals with tuberculosis, chronic nephritis, cushingoid syndrome, or peptic ulcers.

(v) Not for use in horses intended for food.

(vi) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[41 FR 28265, July 9, 1976]

EDITORIAL NOTE: For FEDERAL REGISTER citations affecting § 522.540, see the List of CFR Sections Affected in the Finding Aids section of this volume.

§ 522.542 Dexamethasone-21-isonicotinate suspension.

(a) *Specifications.* Each milliliter of sterile suspension contains 1 milligram of dexamethasone-21-isonicotinate.

(b) *Sponsor.* No. 000010 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used in the treatment of various inflammatory conditions associated with the musculoskeletal system in dogs, cats, and horses.

(2) It is recommended for intramuscular administration as follows: Dogs—0.25 to 1 milligram; cats—0.125 to 0.5 milligram; horses—5 to 20 milligrams. Dosage may be repeated.

(3) Clinical and experimental data have demonstrated that corticosteroids administered orally or parenterally to animals may induce the first stage of parturition when administered during the last trimester of pregnancy and may precipitate premature parturition following by dystocia, fetal death, retained placenta, and metritis.

(4) Not for use in horses intended for food.

(5) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[42 FR 37543, July 22, 1977, as amended at 47 FR 14703, Apr. 6, 1982]

§ 522.562 Diatrizoate meglumine injection.

(a) *Specifications.* Diatrizoate meglumine injection contains 60 percent diatrizoate meglumine in sterile aqueous solution.

(b) *Sponsor.* See No. 000934 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is indicated for use in dogs and cats as an aid to radiographic delineation of internal structures, excretory urography, angiocardiology, and cystography.

(2) For excretory urography administer 0.5 to 1 milliliter per pound of body weight intravenously at the rate of 1 milliliter per second. For angiocardiology administer 0.5 to 1 milliliter per pound of body weight directly into the heart via catheter or intraventricular puncture. For cystography administer via urethral catheter directly into the bladder 10 to 30 milliliters; 1 to 1 or 1 to 10 dilution, 150 milliliters to dogs or 30 milliliters to cats.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[41 FR 30326, July 23, 1976, as amended at 42 FR 36995, July 19, 1977]

§ 522.563 Diatrizoate meglumine and diatrizoate sodium injection.

(a) *Specifications.* Diatrizoate meglumine and diatrizoate sodium injection contains 34.3 percent diatrizoate meglumine and 35 percent diatrizoate sodium, or 66 percent diatrizoate meglumine and 10 percent diatrizoate sodium, in sterile aqueous solution.

(b) *Sponsor.* See No. 053501 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is indicated for use in dogs and cats for visualization in excretion urography, including renal angiography, urethrography, cystography, and urethrography; aortography; angiocardiology; peripheral arteriography, and venography; selective coronary arteriography; cerebral angiography; lymphography; arthrography; discography; and sialography. It is also useful as an aid in delineating peritoneal hernias and fistulous tracts.

(2) For excretion urography administer 0.5 to 1.0 milliliter per pound of body weight to a maximum of 30 milliliters intravenously. For cystography remove urine, administer 5 to 25 milliliters directly into the bladder via catheter. For urethrography administer 1.0 to 5 milliliters via catheter into the urethra to provide desired contrasts delineation. For angiocardiology (including aortography) rapidly inject 5 to 10 milliliters directly into

the heart via catheter or intraventricular puncture. For cerebral angiography rapid injection of 3 to 10 milliliters via carotid artery. For peripheral arteriography and/or venography and selective coronary arteriography rapidly inject 3 to 10 milliliters intravascularly into the vascular bed to be delineated. For lymphography slowly inject 1.0 to 10 milliliters directly into the lymph vessel to be delineated. For arthrography slowly inject 1.0 to 5 milliliters directly into the joint to be delineated. For discography slowly inject 0.5 to 1.0 milliliter directly into the disc to be delineated. For sialography slowly inject 0.5 to 1.0 milliliter into the duct to be delineated. For delineation of fistulous tracts slowly inject quantity necessary to fill the tract. For delineation of peritoneal hernias inject 0.5 to 1.0 milliliter per pound of body weight directly into the peritoneal cavity.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(Secs. 512, 701(a), 52 Stat. 1055, 82 Stat. 343-351 (21 U.S.C. 360b, 371(a)))

[44 FR 12993, Mar. 9, 1979, as amended at 50 FR 41489, Oct. 11, 1985]

§ 522.690 Dinoprost tromethamine sterile solution.

(a) *Specifications.* Each milliliter of sterile solution contains the equivalent of 5 milligrams of dinoprost.

(b) *Sponsor.* See No. 000009 in § 510.600(c) of this chapter.

(c) *Special considerations.* Women of child-bearing age, asthmatics, and persons with bronchial and other respiratory problems should exercise extreme caution when handling this product. Dinoprost tromethamine is readily absorbed through the skin and can cause abortion and bronchio-spasms. Accidental spillage on the skin should be washed off immediately with soap and water. Use of this product in excess of the approved dose may result in drug residues. Do not administer to pregnant cattle unless abortion is desired. Do not administer intravenously; this may potentiate adverse reactions.

(d) *Conditions of use—(1) Mares—(i) Amount.* Equivalent of 1 milligram of

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dinoprost per 100 pounds of body weight.

(ii) *Indications.* For its luteolytic effect to control timing of estrus in estrus cycling mares and in clinically anestrus mares that have a corpus luteum.

(iii) *Limitations.* For use once as a single intramuscular injection. Not for use in horses intended for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(2) *Cattle*—(i) *Amount.* 5 milliliters (equivalent to 25 milligrams of dinoprost).

(ii)(a) *Indications.* For its luteolytic effect to control timing of estrus and ovulation in estrus cycling cattle that have a corpus luteum.

(b) *Limitations.* For use in beef cattle and nonlactating dairy heifers, as follows: Inject a dose of 5 milliliters intramuscularly either once or twice at a 10- to 12-day interval. With a single injection, cattle should be bred at the usual time relative to estrus. With the two injections, cattle can be bred after the second injection either at the usual time relative to detected estrus or at about 80 hours after the second injection. Estrus is expected to occur 1 to 5 days after injection if a corpus luteum was present. Cattle that do not become pregnant to breeding at estrus on days 1 to 5 after injection will be expected to return to estrus in about 18 to 24 days. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(iii)(a) *Indications.* For treatment of pyometra (chronic endometritis).

(b) *Limitations.* For intramuscular use as a single injection. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(3) *Nonlactating cattle*—(i) *Amount.* Five milliliters intramuscularly as a single injection.

(ii) *Indications.* For its abortifacient effect in nonlactating cattle.

(iii) *Limitations.* For intramuscular use only, during first 100 days of gestation. Cattle that abort will abort within 35 days after injection. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(4) *Lactating dairy cattle*—(i) *Amount.* Five milliliters intramuscularly as a single injection.

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(ii) *Indications.* For treatment of unobserved (silent) estrus in lactating dairy cattle that have a corpus luteum.

(iii) *Limitations.* Breed cattle as they are detected in estrus. If estrus has not been observed by 80 hours after injection, breed at 80 hours. If cattle return to estrus breed at the usual time relative to estrus. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(5) *Swine*—(i) *Amount.* 2 milliliters (equivalent to 10 milligrams of dinoprost).

(ii) *Indications.* For parturition induction in swine when injected within 3 days of normal predicted farrowing.

(iii) *Limitations.* For use in swine as follows: Inject a dose of 2 milliliters intramuscularly within 3 days of predicted farrowing. The response to treatment varies by individual animals with a mean interval from administration to parturition of approximately 30 hours. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[41 FR 4818, Feb. 2, 1976, as amended at 46 FR 13214, Feb. 20, 1981; 46 FR 39127, July 31, 1981; 48 FR 6331, Feb. 11, 1983; 48 FR 46023, Oct. 11, 1983; 49 FR 4373, Feb. 6, 1984]

§ 522.723 Diprenorphine hydrochloride injection.

(a) *Chemical name.* N-(Cyclopropylmethyl)-6,7,8,14-tetrahydro-7- α -(1-hydroxy-1-methylethyl)-6,14-endoethanonoripavine hydrochloride.

(b) *Specifications.* Each milliliter of diprenorphine hydrochloride injection, veterinary, contains 2 mg of diprenorphine hydrochloride in sterile aqueous solution.

(c) *Sponsors.* See Nos. 010042 and 000693 in § 510.600(c) of this chapter.

(d) *Conditions of use.* (1) The drug is used for reversing the effects of etorphine hydrochloride injection, veterinary, the use of which is provided for in § 522.883, in wild and exotic animals.

(2) It is administered intramuscularly or intravenously at a suitable dosage level depending upon the species.

(3) For use in wild or exotic animals only. Do not use in domestic food-producing animals. Do not use 30 days before, or during, the hunting season in free-ranging wild animals that might be used for food.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian. Distribution is restricted to veterinarians engaged in zoo and exotic animal practice, wildlife management programs and researchers.

[40 FR 13858, Mar. 27, 1975, as amended at 48 FR 16241, Apr. 15, 1983]

§ 522.740 Disophenol sodium injection.

(a) *Chemical name.* Sodium 2,6-diiodo-4-nitrophenoxide.

(b) *Specifications.* The drug is sterile and contains the equivalent of 0.9 or 4.5 percent disophenol in polyethylene glycol 400 and distilled water.

(c) *Sponsor.* See No. 000859 in § 510.600(c) of this chapter.

(d) *Conditions of use.* (1) The drug is used for the treatment of both dogs infested with hookworms (including *Ancylostoma caninum*, *A. braziliense* and *Uncinaria stenocephala*) and cats infested with the hookworm *A. tubaeforme*.

(2) It is administered subcutaneously at a dosage level equivalent to 4.5 milligrams of disophenol per pound of body weight. A second treatment may be indicated 21 days after the initial treatment.

(3) Do not repeat treatment in less than 21 days.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(5) Use for the treatment of dogs infested with hookworms (including *Ancylostoma caninum*, *A. braziliense* and *Uncinaria stenocephala*) is NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

[40 FR 13858, Mar. 27, 1975, as amended at 41 FR 43400, Oct. 1, 1976; 42 FR 41855, Aug. 19, 1977; 45 FR 43402, June 27, 1980; 47 FR 14150, Apr. 2, 1982]

§ 522.775 Doxapram hydrochloride injection.

(a) *Specifications.* The drug is a sterile aqueous solution containing 20 milligrams doxapram hydrochloride per milliliter.

(b) *Sponsor.* See No. 000031 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) Administer to dogs, cats, and horses to stimulate respiration during and after general anesthesia; to speed awakening and return of reflexes after anesthesia. Administer to neonate dogs and cats to initiate respiration following dystocia or caesarean section; to stimulate respiration following dystocia or caesarean section.

(2) For intravenous use in dogs and cats at a dose of 2½ to 5 milligrams of doxapram hydrochloride per pound of body weight in barbiturate anesthesia, 0.5 mg per lb. in gas anesthesia; for intravenous use in horses at 0.25 mg per lb. of body weight in barbiturate anesthesia, 0.2 mg per lb. in inhalation anesthesia, 0.25 mg per lb. with chloral hydrate with or without magnesium sulfate; for subcutaneous, sublingual, or umbilical vein administration in neonate puppies at a dose rate of 1 to 5 mg; for subcutaneous or sublingual use in neonate kittens at 1 to 2 mg. Dosage may be repeated in 15 to 20 minutes if necessary.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 17838, Apr. 23, 1975]

§ 522.784 Doxylamine succinate injection.

(a) *Specifications.* Each milliliter of the drug contains 11.36 mg of doxylamine succinate.

(b) *Sponsor.* See No. 017220 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used in conditions in which antihistaminic therapy may be expected to alleviate some signs of disease in horses, dogs, and cats.¹

¹These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter.

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(2) It is administered to horses at a dosage level of 25 mg per hundred pounds of body weight. It is administered to dogs and cats at a dosage level of 0.5 to 1 mg per pound of body weight. Doses may be repeated at 8 to 12 hours, if necessary, to produce desired effect. Intravenous route is not recommended for dogs and cats and should be injected slowly in horses. Intramuscular and subcutaneous administration should be by divided injection sites.¹

(3) Not for use in horses intended for food.¹

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

[40 FR 13858, Mar. 27, 1975, as amended at 42 FR 60140, Nov. 25, 1977; 46 FR 48642, Oct. 2, 1981]

§ 522.800 Droperidol and fentanyl citrate injection.

(a) *Specifications.* Droperidol and fentanyl citrate injection is a sterile solution containing 20 milligrams of droperidol and 0.4 milligram of fentanyl citrate per cubic centimeter.

(b) *Sponsor.* See No. 000045 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is used in dogs as an analgesic and tranquilizer and for general anesthesia.

(2) It is administered as follows:

(i) For analgesia and tranquilization administer according to response desired, as follows:

(a) Intramuscularly at the rate of 1 cubic centimeter per 15 to 20 pounds of body weight in conjunction with atropine sulfate administered at the rate of 0.02 milligram per pound of body weight, or

(b) Intravenously at the rate of 1 cubic centimeter per 25 to 60 pounds of body weight in conjunction with atropine sulfate administered at the rate of 0.02 milligram per pound of body weight.

(ii) For general anesthesia administer according to response desired, as follows:

(a) Intramuscularly at the rate of 1 cubic centimeter per 40 pounds of body weight in conjunction with atropine sulfate administered at the rate of 0.02 milligram per pound of body weight and followed in 10 minutes by

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an intravenous administration of sodium pentobarbital at the rate of 3 milligrams per pound of body weight, or

(b) Intravenously at the rate of 1 cubic centimeter per 25 to 60 pounds of body weight in conjunction with atropine sulfate administered at the rate of 0.02 milligram per pound of body weight and followed within 15 seconds by an intravenous administration of sodium pentobarbital at the rate of 3 milligrams per pound of body weight.

(3) For use only by or on the order of a licensed veterinarian.

§ 522.820 Erythromycin injection.

(a) *Specifications.* Each milliliter of polyethylene glycol vehicle contains 100 milligrams of erythromycin base with 2 percent butyl aminobenzoate.

(b) *Sponsor.* See 050604 in § 510.600(c) of this chapter.

(c) *NAS/NRC status.* The conditions specified in paragraph (d) of this section have been reviewed by NAS/NRC and are deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(d) *Conditions of use in dogs and cats.*—(1) *Amount.* 3 to 5 milligrams per pound of body weight, intramuscularly, two to three times daily, for up to 5 days.

(2) *Indications for use.*—(i) *Dogs.* For the treatment of bacterial pneumonia, upper respiratory infections (tonsillitis, bronchitis, tracheitis, pharyngitis, pleurisy), endometritis and metritis, and bacterial wound infections caused by *Staphylococcus spp.*, *Streptococcus spp.*, and *Corynebacterium spp.*, sensitive to erythromycin.

(ii) *Cats.* For the treatment of bacterial pneumonia, upper respiratory infections (rhinitis, bronchitis), secondary infections associated with panleukopenia, and bacterial wound infections caused by *Staphylococcus spp.* and *Streptococcus spp.*, susceptible to erythromycin.

(3) *Limitations.* Administer by deep intramuscular injection into the heavy muscles of the neck and limbs. Do not administer intravenously or intraperitoneally. Avoid subcutaneous use. Do

not administer from moist or wet syringe. As with all antibiotics, appropriate in vitro culturing and susceptibility testing of samples taken before treatment should be conducted. Do not administer in conjunction with penicillin. As with all antibiotics, excessive continuous use may result in an overgrowth of nonsusceptible organisms. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[44 FR 20671, Apr. 6, 1979, as amended at 47 FR 14149, Apr. 2, 1982]

§ 522.840 Estradiol.

(a) *Specifications.* Each silicone rubber implant contains 24 or 45 milligrams of estradiol.

(b) *Sponsor.* See 000986 in § 510.600(c) of this chapter.

(c) *Conditions of use.* It is used for implantation in steers and heifers as follows:

(1) *Amount.* Insert one 24-milligram implant every 200 days; insert one 45-milligram implant every 400 days.

(2) *Indications for use.* For increased rate of weight gain in suckling and pastured growing steers; for improved feed efficiency and increased rate of weight gain in confined steers and heifers.

(3) *Limitations.* For subcutaneous ear implantation in steers and heifers only. A second implant may be used if desired. No additional effectiveness may be expected from reimplanting in less than 200 days for the 24-milligram implant or 400 days for the 45-milligram implant. Increased sexual activity (bulling, riding, and excitability) has been reported in implanted animals.

[51 FR 22276, June 19, 1986]

§ 522.842 Estradiol benzoate and testosterone propionate in combination.

(a) *Chemical names.* (1) Estradiol benzoate: 1,3,5(10)-Estratriene-3,17 beta-diol 3-benzoate.

(2) Testosterone propionate: 17beta-Hydroxyandrost-4-en-3-one propionate.

(b) *Sponsor.* See Nos. 000033 and 021641 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See §§ 556.240 and 556.710 of this chapter.

(d) *Conditions of use.* It is used for implantation in heifers as follows:

(1) *Amount.* 20 milligrams of estradiol benzoate and 200 milligrams of testosterone propionate per dose.

(2) *Indications for use.* Growth promotion and improved feed efficiency.

(3) *Limitations.* For heifers weighing 400 pounds or more; for subcutaneous ear implantation, one dose per animal; not for use in dairy or beef replacement heifers.

(e) *NAS/NRC status.* These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety data.

[40 FR 13858, Mar. 27, 1975, as amended at 49 FR 29778, July 24, 1984]

§ 522.850 Estradiol valerate and norgestomet in combination.

(a) *Specifications.* The product is a two-component drug consisting of the following:

(1) An implant containing 6.0 milligrams of norgestomet.

(2) An injectable solution (sesame oil) containing 3.0 milligrams of norgestomet and 5.0 milligrams of estradiol valerate per 2 milliliters.

(b) *Sponsor.* See 050604 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* One implant and 2 milliliters of injection at time of implantation.

(2) *Indications for use.* For synchronization of estrus/ovulation in cycling beef cattle and non-lactating dairy heifers.

(3) *Limitations.* Insert implant subcutaneously in the ear only; then immediately inject solution intramuscularly only. Counting the day of implantation as day 1, remove the implant on day 10. Collect all implants as they are removed and burn them. While animals are restrained for artificial insemination, avoid other treatments such as vaccinations, dipping, pour-on grub and louse prevention, spraying, etc. When inseminating without estrus detection, the entire treated group should be started at 48 hours after the last implant has been removed and should be completed

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within 6 hours. Where estrus detection is preferred, insemination should be approximately 12 hours after first detection of estrus. Those that do not conceive can be re-bred when they return to estrus approximately 17 to 25 days after implant removal. Do not use in cows producing milk for human consumption.

[47 FR 55477, Dec. 10, 1982, as amended at 48 FR 49656, Oct. 27, 1983; 51 FR 33592, Sept. 22, 1986; 54 FR 1165, Jan. 12, 1989]

§ 522.863 Ethylisobutrazine hydrochloride injection.

(a) *Specifications.* The drug is a sterile aqueous solution. Each milliliter contains 50 milligrams of ethylisobutrazine hydrochloride.

(b) *Sponsor.* See No. 017220 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is used in dogs as a tranquilizer.¹

(2) It is administered intramuscularly at a dosage level of 2 to 5 milligrams of ethylisobutrazine hydrochloride per pound of body weight for profound tranquilization. It is administered intravenously at a dosage level of 1 to 2 milligrams of ethylisobutrazine hydrochloride per pound of body weight to effect.¹

(3) It is not to be used in conjunction with organophosphates and/or procaine hydrochloride because phenothiazines may potentiate the toxicity of organophosphates and the activity of procaine hydrochloride.¹

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

[40 FR 13858, Mar. 27, 1975, as amended at 46 FR 48642, Oct. 2, 1981]

§ 522.883 Etorphine hydrochloride injection.

(a) *Chemical name.* 6,7,8,14 - tetrahydro - alpha - methyl - alpha - propyl - 6,14 - endo-ethenooripavine-alpha-methanol hydrochloride.

(b) *Specifications.* Each milliliter of etorphine hydrochloride injection, vet-

¹These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

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erinary, contains 1 mg of etorphine hydrochloride in sterile aqueous solution.

(c) *Sponsors.* See Nos. 010042 and 000693 in § 510.600(c) of this chapter.

(d) *Conditions of use.* (1) The drug is used for the immobilization of wild and exotic animals.

(2) It is administered intramuscularly by hand syringe or syringe dart at a suitable dosage level depending upon the species.

(3) Do not use the drug unless diprenorphine hydrochloride injection, veterinary, as provided for in § 522.723, is available for use in reversing the effects of etorphine hydrochloride injection, veterinary.

(4) For use in wild or exotic animals only. Do not use in domestic food-producing animals. Do not use 30 days before, or during, the hunting season in free-ranging wild animals that might be used for food.

(5) Federal law restricts this drug to use by or on the order of a licensed veterinarian. Distribution is restricted to veterinarians engaged in zoo and exotic animal practice, wildlife management programs, and researchers.

[40 FR 13858, Mar. 27, 1975, as amended at 48 FR 16241, Apr. 15, 1983]

§ 522.900 Euthanasia solution.

(a)(1) *Specifications.* Each milliliter contains 200 milligrams of N-[2-(methoxy-phenyl)-2-ethyl-butyl-(1)]-gamma-hydroxybutyramide, 50 milligrams of 4, 4'-methylene-bis(cyclohexyl-trimethyl-ammonium iodide), 5 milligrams of tetracaine hydrochloride, with 0.6 milliliter dimethylformamide in distilled water.

(2) *Sponsor.* No. 012799 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) The drug is used for the humane euthanasia of animals without excitation or pain. It is used in dogs, cats, horses, mink, small laboratory animals (mice, rats, guinea pigs, and rabbits) and birds (pigeons and parakeets).

(ii) *Dosage—(a) Dogs.* Intravenous or intracardiac injection: Use 0.3 milliliter/kilogram (0.14 milliliter/pound). Intrapulmonary injection: For animals weighing up to 10 kilograms, use 7 to 10 milliliters. In larger animals, follow

initial 10 milliliters by another 3 to 10 milliliters by intrapulmonary or intracardiac administration.

(b) *Cats*. Intravenous injection: Use 0.3 milliliter/kilogram (0.14 milliliter/pound). Intrapulmonary injection: Kittens a few days old, 1 milliliter; kittens up to 6 months of age, 3 milliliters; cats over 6 months of age, 5 milliliters; cats weighing more than 5 kilograms (11 pounds), 10 milliliters.

(c) *Horses*. Intravenous injection: Use 4 to 6 milliliters/50 kilograms (110 pounds of body weight).

(d) *Mink*. Intraperitoneal injection: 0.5 to 1 milliliter.

(e) *Birds and small laboratory animals*. Intrapulmonary injection: 0.5 to 2 milliliters.

(iii) Not to be used for therapeutic purposes.

(iv) Do not use in animals intended for food.

(v) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(b)(1) *Specifications*. Each milliliter of nonsterile solution contains 390 milligrams of pentobarbital sodium and 50 milligrams of phenytoin sodium.

(2) *Sponsor*. No. 000061 in § 510.600(c) of this chapter.

(3) *Conditions of use*—(i) *Indications for use*. For the humane, painless, and rapid euthanasia of dogs.

(ii) *Amount*. One milliliter (390 milligrams of pentobarbital sodium and 50 milligrams of phenytoin sodium) for each 10 pounds of body weight.

(iii) *Limitations*. For intravenous injection or intracardiac injection when intravenous use is impractical. Do not use for therapeutic purposes. Do not use in animals intended for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(c)(1) *Specifications*. Each milliliter of nonsterile, aqueous solution contains 400 milligrams of secobarbital sodium and 25 milligrams of dibucaine hydrochloride.

(2) *Sponsor*. See 000033 in § 510.600(c) of this chapter.

(3) *Conditions of use*—(i) *Indications for use*. To induce rapid, humane, painless euthanasia of dogs.

(ii) *Amount*. For dogs, 1 milliliter for each 10 pounds of body weight.

(iii) *Limitations*. For intravenous injection. Do not use for therapeutic purposes. Do not use in animals intended for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[46 FR 23232, Apr. 24, 1981, as amended at 47 FR 15327, Apr. 9, 1982; 48 FR 16241, Apr. 15, 1983; 52 FR 7832, Mar. 13, 1987]

§ 522.914 Fenprostalene solution.

(a) *Specifications*—(1) *Cattle*. Each milliliter of sterile solution contains 0.5 milligram of fenprostalene.

(2) *Swine*. Each milliliter of sterile solution contains 0.25 milligram of fenprostalene.

(b) *Sponsor*. See 000033 in § 510.600(c) of this chapter.

(c) *Related tolerances*. See § 556.277 of this chapter.

(d) *Special considerations*. Labeling shall bear the following statements: Women of childbearing age, asthmatics, and persons with bronchial and other respiratory problems should exercise extreme caution when handling this product. It is readily absorbed through the skin and may cause abortion and/or bronchospasms. Accidental spillage on the skin should be washed off immediately with soap and water.

(e) *Conditions of use*—(1) *Cattle*—(i) *Amount*. 1 milligram (2 milliliters) subcutaneously per animal.

(ii) *Indications for use*. For feedlot heifers to induce abortion when pregnant 150 days or less. For beef or nonlactating dairy cattle for estrus synchronization.

(iii) *Limitations*. Subcutaneous use in cattle only. Feedlot heifers to induce abortion, single dose. Beef or nonlactating dairy cattle for estrus synchronization, a single dose or two doses 11 to 13 days apart. Do not use in pregnant animals unless abortion is desired. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(2) *Swine*—(i) *Amount*. 0.25 milligram (1 milliliter) subcutaneously once per animal.

(ii) *Indications for use*. For sows and gilts pregnant at least 112 days for the induction of parturition.

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(iii) *Limitations.* Subcutaneous use in swine only. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[48 FR 7161, Feb. 18, 1983, as amended at 49 FR 26715, June 29, 1984; 54 FR 400, Jan. 6, 1989]

§ 522.940 Colloidal ferric oxide injection.

(a) *Specifications.* Each milliliter of the drug contains colloidal ferric oxide equivalent to 100 milligrams of iron stabilized with a low-viscosity dextrin and contains 0.5 percent phenol as a preservative.

(b) *NAS/NRC status.* Use of this drug has been NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(c)(1) *Sponsor.* See Nos. 010042 and 017800 in § 510.600(c) of this chapter.

(2) *Conditions of use.* It is used in baby pigs as follows:

(i) For the prevention of anemia due to iron deficiency, administer an initial intramuscular injection of 1 milliliter of the drug to each animal at any time between 2 to 5 days of age. Dosage may be repeated at 2 weeks of age.

(ii) For the treatment of anemia due to iron deficiency, administer an intramuscular injection of from 1 to 2 milliliters of the drug to each animal at any time between 5 to 28 days of age.

[40 FR 13858, Mar. 27, 1975, as amended at 49 FR 38938, Oct. 2, 1984; 50 FR 23298, June 3, 1985; 50 FR 25216, June 18, 1985; 51 FR 14989, Apr. 22, 1986; 51 FR 18314, May 19, 1986]

§ 522.960 Flumethasone implantation or injectable dosage forms.

[44 FR 16011, Mar. 16, 1979]

§ 522.960a Flumethasone suspension.

(a) *Chemical name.* 6 α ,9 α -Difluoro-11 β ,17,21 - trihydroxy - 16 α - methylpregna - 1,4 - diene - 3,20 - dione.

(b) *Specifications.* Flumethasone suspension is sterile and each milliliter of the drug contains: 2 milligrams of flumethasone, 20 milligrams of propylene glycol, 9 milligrams of benzyl alcohol (as preservative), 8 milligrams of

sodium chloride, 0.02 milligram of polysorbate-80, 0.1 milligram of citric acid, and water for injection q.s.

(c) *Sponsor.* See No. 000033 in § 510.600(c) of this chapter.

(d) *Conditions of use.* (1) It is recommended in the various disease states involving synovial structures (joints) of horses where excessive synovial fluid of inflammatory origin is present and where permanent structural changes do not exist. Such conditions include arthritis, carpalitis, and osselet.

(2) The drug is administered intravenously at a dosage level of 6 to 12 milligrams per injection. The dosage level is dependent upon the size of the involved synovial structure and the degree of severity of the condition under treatment. The dosage is limited to a single injection per week in any one synovial structure.

(3) Clinical and experimental data have demonstrated that corticosteroids administered orally and parenterally to animals during the last trimester of pregnancy may induce the first stage of parturition and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis. The drug is not to be used in horses intended for slaughter for food purposes.

(4) For use only by or on the order of a licensed veterinarian.

[40 FR 13858, Mar. 27, 1975. Redesignated at 44 FR 16011, Mar. 16, 1979]

§ 522.960b Flumethasone acetate injection.

(a) *Chemical name.* 6 α ,9 α -Difluoro - 16 - alpha - methylprednisolone 21-acetate.

(b) *Specifications.* Flumethasone injection is sterile and contains per cubic centimeter: 2 milligrams of flumethasone acetate; 20 milligrams of propylene glycol; 9 milligrams of benzyl alcohol (as preservative); 8 milligrams of sodium chloride; 1 milligram of polysorbate 80; 0.1 milligram of citric acid and water for injection q.s.

(c) *Sponsor.* See No. 000033 in § 510.600(c) of this chapter.

(d) *Conditions of use.* (1) It is recommended in certain acute and chronic canine dermatoses of varying etiology to help control the pruritus, irritation

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and inflammation associated with these conditions.

(2) The drug is administered intramuscularly at the following recommended daily dosage:

Weight of animal in pounds	Dosage in milligrams
Up to 10.....	1.0
10 to 25.....	2.0
25 and over.....	4.0

Dosage should be adjusted according to the weight of the animal, the severity of the symptoms, and the response noted. Dosage by injection should not exceed 3 days of therapy. With chronic conditions intramuscular therapy may be followed by oral administration of flumethasone tablets at a daily dose of from 0.0625 to 0.25 milligram per animal.

(3) For use only by or on the order of a licensed veterinarian.

[40 FR 13858, Mar. 27, 1975. Redesignated at 44 FR 16011, Mar. 16, 1979]

§ 522.960c Flumethasone solution.

(a) *Specifications.* Each milliliter of sterile aqueous solution contains 0.5 milligram flumethasone.

(b) *Sponsor.* See No. 000033 in § 510.600(c) of this chapter.

(c) *Conditions of use.* It is used as follows:

(1) *Horses*—(i) *Amount.* 1.25 to 2.5 milligrams daily, intravenously, intramuscularly, or intra-articularly.

(ii) *Indications for use.* It is used for the treatment of musculoskeletal conditions due to inflammation, where permanent structural changes do not exist, e.g., bursitis, carpalitis, osselets, and myositis; and allergic states, e.g., hives, urticaria, and insect bites.

(iii) *Limitations*—(a) Clinical and experimental data have demonstrated that corticosteroids administered orally or parenterally to animals may induce the first stage of parturition when administered during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis.

(b) When a long-term therapy is used, the dose should be individually adjusted to the minimum maintenance

dose. A protein-rich diet is useful in dogs and cats on long-term therapy to counteract nitrogen loss if it should occur. A small amount of potassium chloride daily in the diet will counteract excessive potassium loss if this is present.

(c) It has been demonstrated that corticosteroids, especially at high dose levels, may result in delayed wound and fracture healing.

(d) Flumethasone may be administered to animals with bacterial diseases provided appropriate antibacterial therapy is administered simultaneously.

(e) The drug is not to be used in horses intended for slaughter for food purposes.

(f) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(2) *Dogs*—(i) *Amount.* 0.0625 to 0.25 milligram daily, intravenously, intramuscularly, or subcutaneously; 0.125 to 1.0 milligram daily, intralesionally, depending on the size and location of the lesion; 0.166 to 1.0 milligram daily, intra-articularly, depending on the severity of the condition and the size of the involved joint.

(ii) *Indications for use.* It is used for the treatment of musculoskeletal conditions due to inflammation of muscles or joints and accessory structures where permanent structural changes do not exist, e.g., arthritis, osteoarthritis, disc syndrome, and myositis (in septic arthritis, appropriate antibacterial therapy should be concurrently administered); certain acute and chronic dermatoses of varying etiology to help control associated pruritus, irritation, and inflammation; otitis externa in conjunction with topical medication; allergic states, e.g., hives, urticaria, and insect bites; and shock and shock-like states by intravenous administration.

(iii) *Limitations.* See paragraph (c)(1)(iii) of this section.

(3) *Cats*—(i) *Amount.* 0.03125 to 0.125 milligram daily intravenously, intramuscularly, or subcutaneously.

(ii) *Indications for use.* It is used for the treatment of certain acute and chronic dermatoses of varying etiology to help control associated pruritus, irritation, and inflammation.

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(iii) *Limitations.* See paragraph (c)(1)(iii) of this section.

[44 FR 16011, Mar. 16, 1978]

§ 522.970 Flunixin meglumine solution.

(a) *Specifications.* The drug contains 50 milligrams of flunixin per milliliter of aqueous solution.

(b) *Sponsor.* No. 000061 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* 0.5 milligram of flunixin per pound of body weight (1 milliliter per 100 pounds) per day.

(2) *Indications for use.* Horses: For alleviation of inflammation and pain associated with musculoskeletal disorders, and alleviation of pain associated with colic.

(3) *Limitations.* For musculoskeletal disorders, administer intravenously or intramuscularly for up to 5 days. For colic, administer a single dose intravenously—the single dose may be repeated if signs of colic recur. Caution: The effect of this drug on pregnancy has not been determined. Not for use in horses intended for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[42 FR 39103, Aug. 2, 1977, as amended at 52 FR 7832, Mar. 13, 1987]

§ 522.995 Fluprostenol sodium injection.

(a) *Specifications.* Each milliliter of sterile aqueous solution contains fluprostenol sodium equivalent to 50 micrograms of fluprostenol.

(b) *Sponsor.* See 000859 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* 0.55 microgram fluprostenol per kilogram of body weight.

(2) *Indications for use.* The drug is used in mares for its luteolytic effect to control the timing of estrus in estrous cycling and in clinically anestrous mares that have a corpus luteum.

(3) *Limitations.* Administer by intramuscular injection only. *Warning:* Not for use in horses intended for food. For veterinary use only. Federal law restricts this drug to use by or on the order of a licensed veterinarian. Women of childbearing age, asthmatics, and persons with bronchial and other respiratory problems should ex-

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ercise extreme caution when handling this product. In the early stages, women may be unaware of their pregnancies. Fluprostenol is readily absorbed through the skin and can cause abortion and/or bronchospasms. Direct contact with the skin should therefore be avoided. Accidental spillage on the skin should be washed off immediately with soap and water.

[44 FR 52191, Sept. 7, 1979, as amended at 47 FR 22092, May 21, 1982]

§ 522.1010 Furosemide injection.

(a) *Specifications.* Each milliliter of sterile solution contains 50 milligram of furosemide as the diethanolamine salt.

(b) *Sponsor.* See No. 012799 in § 510.600(c) of this chapter for use in dogs and cats as in paragraph (c)(1) of this section, horses as in paragraph (c)(2)(i) of this section, and cattle as in paragraph (c)(3) of this section. See Nos. 000864 and 054273 in § 510.600(c) for use in horses as in paragraph (c)(2)(ii) of this section. See No. 054273 in § 510.600(c) of this chapter for use in dogs as in paragraph (c)(1) of this section.

(c) *Conditions of use—(1) Dogs and cats.* (i) It is used for the treatment of edema (pulmonary congestion, ascites) associated with cardiac insufficiency and acute noninflammatory tissue edema.

(ii) The drug is administered intramuscularly or intravenously at a dosage of 12.5 to 25 milligrams per 100 pounds of body weight; once or twice daily after a 6- to 8-hour interval. The lower dosage is suggested for cats. The dosage should be adjusted to the individual animal's response. In refractory or severe edematous cases, the dosage may be doubled or increased by increments of 1 milligram per pound of body weight to establish the effective dose. The established effective dose should be administered once or twice daily on an intermittent daily schedule. Diuretic therapy should be discontinued after reduction of edema, when necessary, maintained after determining a programmed dosage schedule to prevent recurrence.

(2) *Horses.* (i) It is used for the treatment of edema (pulmonary conge-

tion, ascites) associated with cardiac insufficiency and acute noninflammatory tissue edema.

(a) Administer intramuscularly or intravenously at 250 to 500 milligrams per animal once or twice daily at 6- to 8-hour intervals until desired results are achieved.

(b) Do not use in horses intended for food.

(ii) It is used for treatment of acute noninflammatory tissue edema.

(a) Administer intramuscularly or intravenously at 0.5 milligram per pound of body weight (1.0 milligram per kilogram); once or twice daily at 6- to 8-hour intervals.

(b) The dosage should be adjusted to the individual's response. In refractory or severe edematous cases, the dosage may be doubled or increased by increments of 1 milligram per pound of body weight to establish the effective dose. The established effective dose should be administered once or twice daily on an intermittent daily schedule, i.e., every other day or 2 to 4 consecutive days weekly. Concurrent therapy for treatment of systemic conditions causing edema (pulmonary congestion, ascites, cardiac insufficiency) should be instituted.

(3) *Cattle.* (i) It is used for the treatment of physiological parturient edema of the mammary gland and associated structures.

(ii) The drug is administered intramuscularly or intravenously at a dosage of 500 milligrams per animal once daily or 250 milligrams per animal twice daily at 12-hour intervals, treatment not to exceed 48 hours postparturition.

(iii) Milk taken during treatment and for 48 hours (four milkings) after the last treatment must not be used for food.

(iv) Cattle must not be slaughtered for food within 48 hours following last treatment.

(4) The drug if given in excessive amounts may result in dehydration and electrolyte imbalance.

(5) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 60051, Dec. 31, 1975, as amended at 41 FR 10426, Mar. 11, 1976; 48 FR 36572,

Aug. 12, 1983; 49 FR 26715, June 29, 1984; 53 FR 40727, Oct. 18, 1988]

§ 522.1020 Gelatin solution.

(a) *Specifications.* It is sterile and each 100 cubic centimeters contains 8 grams of gelatin in an 0.85 percent sodium chloride solution.

(b) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is used to restore circulatory volume and maintain blood pressure in animals being treated for shock.

(2) The exact dosage to be administered must be determined after evaluating the animal's condition and will vary according to the size of the animal and the degree of shock. A suggested dosage range for small animals such as dogs is 4 to 8 cubic centimeters per pound body weight. The suggested dosage range for large animals such as sheep, calves, cows, or horses is 2 to 4 cubic centimeters per pound of body weight. It is administered intravenously at a rate of 10 cubic centimeters per minute in small animals and 20 to 30 cubic centimeters per minute in large animals. The solution is administered aseptically and must be between 50° to 70° F. when injected.

(3) A few animals will exhibit signs of allergic reaction. This solution can cause transient reversible nephrosis. This product is not intended to replace whole blood in cases of anemia and should not be used in the presence of renal dysfunction. Unused portions remaining in bottles should be discarded.

(4) For use only by or on the order of a licensed veterinarian.

§ 522.1044 Gentamicin sulfate injection.

(a) *Specifications.* Each milliliter of sterile aqueous solution contains the equivalent of either 5 or 50 milligrams of gentamicin.

(b) *Sponsors.* (1) See No. 000061 in § 510.600(c) of this chapter for use of 5 milligram-per-milliliter solution in swine as in paragraph (d)(4) of this section and for use of 50 milligram-per-milliliter solution in dogs, cats, and chickens as in paragraphs (d) (1) and (3) of this section.

(2) See No. 000138 for use of 5 milligram-per-milliliter solution in turkeys as in paragraph (d)(2) of this section.

(3) See No. 054273 for use of 50 milligram-per-milliliter solution in dogs as in paragraph (d)(5) of this section.

(c) *Related tolerances.* See § 556.300 of this chapter.

(d) *Conditions of use*—(1) *Dogs and cats*—(i) *Amount.* Two milligrams of gentamicin per pound of body weight, twice daily on the first day, once daily thereafter, using a 50 milligram-per-milliliter solution.

(ii) *Indications for use*—(a) *Dogs.* For the treatment of infections of urinary tract (cystitis, nephritis), respiratory tract (tonsillitis, pneumonia, tracheobronchitis), skin and soft tissue (pyodermitis, wounds, lacerations, peritonitis).

(b) *Cats.* For the treatment of infections of urinary tract (cystitis, nephritis), respiratory tract (pneumonitis, pneumonia, upper respiratory tract infections), skin and soft tissue (wounds, lacerations, peritonitis), and as supportive therapy for secondary bacterial infections associated with panleucopenia.

(iii) *Limitations.* Administer intramuscularly or subcutaneously. If response is not noted after 7 days, the antibiotic sensitivity of the infecting organism should be retested. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(2) *Turkeys*—(i) *Amount.* One milligram of gentamicin per poult, using a 5 milligram-per-milliliter solution.

(ii) *Indications for use.* As an aid in the prevention of early mortality due to Arizona paracolon infections susceptible to gentamicin.

(iii) *Limitations.* For 1- to 3-day old turkey poults. Administer subcutaneously in the neck. Injected poults must not be slaughtered for food for at least 9 weeks after treatment.

(3) *Chickens*—(i) *Amount.* 0.2 milligram of gentamicin per 0.2 milliliter dose, using a 50 milligram-per-milliliter solution diluted with sterile physiological saline to 1.0 milligram per milliliter.

(ii) *Indications for use.* In day-old chickens, for prevention of early mortality caused by *Escherichia coli*, *Salmonella typhimurium*, and *Pseudomonas aeruginosa* that are susceptible to gentamicin.

(iii) *Limitations.* For use in day-old chickens only. Administer aseptically injecting the diluted product subcutaneously in the neck. Do not slaughter treated animals for food for at least 5 weeks after treatment.

(4) *Swine*—(i) *Amount.* 5 milligrams of gentamicin as a single intramuscular dose using 5 milligram-per-milliliter solution.

(ii) *Indications for use.* In piglets to 3 days old for treatment of porcine colibacillosis caused by strains of *coli* sensitive to gentamicin.

(iii) *Limitations.* For single intramuscular dose in pigs up to 3 days of age only. Do not slaughter treated animals for food for at least 40 days following treatment.

(5) *Dogs*—(i) *Amount.* 2 milligrams gentamicin per pound of body weight twice daily on the first day, then once daily.

(ii) *Indications for use.* For use in the treatment of urinary tract infections (cystitis) caused by *Proteus mirabilis*, *Escherichia coli*, and *Staphylococcus aureus*.

(iii) *Limitations.* Administer intramuscularly or subcutaneously. If improvement is seen after 3 days of treatment should be discontinued and the diagnosis reevaluated. Treatment not to exceed 7 days. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[43 FR 1942, Jan. 13, 1978, as amended at 43 FR 791, Jan. 7, 1983; 51 FR 15606, Apr. 1986; 52 FR 7832, Mar. 13, 1987; 53 FR 40727, Oct. 18, 1988]

§ 522.1055 Gleptoferron injection.

(a) *Specifications.* Each milliliter contains the equivalent of 200 milligrams of elemental iron as gleptoferron (complex of ferric hydroxide and dextran glucoheptonic acid), and percent phenol as a preservative.

(b) *Sponsor.* See 012525 § 510.600(c) of this chapter.

(c) *Conditions of use.* It is used in baby pigs as follows:

(1) For prevention of iron deficiency anemia, administer 200 milligrams elemental iron intramuscularly on or before 3 days of age.

(2) For treatment of iron deficiency anemia, administer 200 milligrams of elemental iron intramuscularly.

[45 FR 61288, Sept. 16, 1980]

§ 522.1060 Glyceryl guaiacolate implantation or injectable dosage forms. [Reserved]

[41 FR 48732, Nov. 5, 1976]

§ 522.1060a Glyceryl guaiacolate sterile powder.

(a) *Specifications.* Complies with N.F. XIII.

(b) *Sponsor.* See No. 037990 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is indicated for intravenous use as a muscle relaxant in horses.

(2) A 5 percent solution is prepared by dissolving 50 grams of the drug in sterile water for injection to make 1 liter of solution. It is administered by rapid intravenous infusion at a fixed dosage of 1 milliliter of prepared solution per pound of body weight.

(3) Not to be used in horses intended for food.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13858, Mar. 27, 1975. Redesignated at 41 FR 48732, Nov. 5, 1976]

§ 522.1060b Glyceryl guaiacolate injection.

(a) *Specifications.* Each milliliter of sterile aqueous solution contains 50 milligrams of glyceryl guaiacolate and 50 milligrams of dextrose.

(b) *Sponsor.* See No. 037990 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used intravenously as a skeletal muscle relaxant in horses.

(2) Administer rapidly at a dosage of 1 milliliter per pound of body weight.

(3) Not to be used in horses intended for food.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[41 FR 48732, Nov. 5, 1976, as amended at 52 FR 7832, Mar. 13, 1987]

§ 522.1066 Glycopyrrolate injection.

(a) *Specifications.* Each milliliter of aqueous solution contains 0.2 milligram of glycopyrrolate.

(b) *Sponsor.* See No. 000031 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is indicated as a preanesthetic agent in dogs and cats.

(2) It is administered intravenously, intramuscularly, or subcutaneously in dogs and intramuscularly in cats at a dosage level of 5 micrograms per pound of body weight (0.25 milliliter per 10 pounds of body weight).

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[48 FR 21567, May 13, 1983]

§ 522.1078 Gonadorelin diacetate tetrahydrate injection

(a) *Specifications.* The drug contains 50 micrograms of gonadorelin diacetate tetrahydrate in each milliliter of sterile solution.

(b) *Sponsor.* See No. 050604 in § 510.600(c) of this chapter.

(c) *Conditions of use.* It is used in dairy cows as follows:

(1) *Amount.* 100 micrograms per cow.

(2) *Indications for use.* The drug is used for the treatment of ovarian cysts.

(3) *Limitations.* Administer as a single intramuscular or intravenous injection. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[43 FR 9804, Mar. 10, 1978, as amended at 45 FR 56798, Aug. 26, 1980]

§ 522.1081 Chorionic gonadotropin for injection; chorionic gonadotropin suspension.

(a)(1) *Specifications.* Chorionic gonadotropin for injection is supplied in vials containing 5,000, 10,000 or 20,000 U.S.P. units of lyophilized powder for reconstitution with the accompanying sterile diluent to a 10 milliliter solution.

(2) *Sponsor.* See sponsor numbers in § 510.600(c) of this chapter, as follows:

(i) Nos. 000402 and 053501 for use of 10,000 U.S.P. units intramuscularly, 2,500 to 5,000 U.S.P. units intravenously, and 500 to 2,500 U.S.P. units intrafollicularly.

(ii) Nos. 000469 and 032420 for use of 10,000 U.S.P. units intramuscularly

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and 500 to 2,500 U.S.P. units intrafollicularly.

(3) *Conditions of use*—(i) *Amount*. (a) 10,000 U.S.P. units as a single, deep intramuscular injection.¹

(b) 500 to 2,500 U.S.P. units for intrafollicular injection.¹

(c) 2,500 to 5,000 U.S.P. units intravenously.

(ii) *Indications for use*. For parenteral use in cows for treatment of nymphomania (frequent or constant heat) due to cystic ovaries.¹

(iii) *Limitations*. Dosage may be repeated in 14 days if the animal's behavior or rectal examination of the ovaries indicates the necessity for retreatment. Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

(b)(1) *Specifications*. Chorionic gonadotropin suspension, veterinary contains in each milliliter, 750 I.U. of chorionic gonadotropin suspended in white wax and sesame oil.

(2) *Sponsor*. See No. 000986 in § 510.600(c) of this chapter.

(3) *Conditions of use*—(i) *Amount*. 2 milliliters (1,500 I.U.) subcutaneously, at the time of insemination, in the neck or shoulder region.

(ii) *Indications for use*. The drug is used as an aid in increasing pregnancy rate of estrus-synchronized and normal cycling heifers.

(iii) *Limitations*. The drug is not to be used to induce multiple ovulations. Doses higher than recommended may reduce pregnancy rate. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[42 FR 58167, Nov. 8, 1977, as amended at 45 FR 81038, Dec. 9, 1980; 50 FR 41489, Oct. 11, 1985; 50 FR 45603, Nov. 1, 1985; 52 FR 25212, July 6, 1987]

§ 522.1085 Guaifenesin sterile powder.

(a) *Specifications*. It is a sterile powder containing guaifenesin.

(b) *Sponsor*. See No. 000031 in § 510.600(c) of this chapter.

(c) *Conditions of use*. (1) It is indicated for intravenous use as a muscle relaxant in horses.

¹ These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified at § 514.111 of this chapter.

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(2) A solution is prepared by dissolving the drug in sterile water for injection to make a solution containing 1 milligram of guaifenesin per milliliter of solution. It is administered by rapid intravenous infusion at a fixed dosage of 1 milliliter of prepared solution per pound of body weight.

(3) Not to be used in horses intended for food.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[49 FR 48039, Dec. 10, 1984]

§ 522.1145 Hyaluronate sodium injection

(a)(1) *Specifications*. Each milliliter of sterile aqueous solution contains 10 milligrams of hyaluronate sodium.

(2) *Sponsors*. See 000016 and 05321 in § 510.600(c) of this chapter.

(3) *Conditions of use*—(i) *Amount*. Small and medium-size joints (carpometacarpal fetlock)—20 milligrams; larger joints (hock)—40 milligrams.

(ii) *Indications for use*. Treatment of joint dysfunction in horses due to non-infectious synovitis associated with equine osteoarthritis.

(iii) *Limitations*. For intra-articular injection in horses only. Treatment may be repeated at weekly intervals for a total of three treatments. Not for use in horses intended for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(b)(1) *Specifications*. Each milliliter of sterile aqueous solution contains 10 milligrams of hyaluronate sodium.

(2) *Sponsor*. See 053501 in § 510.600(c) of this chapter.

(3) *Conditions of use*—(i) *Amount*. Small and medium-size joints (carpometacarpal fetlock)—10 milligrams; larger joints (hock)—20 milligrams.

(ii) *Indications for use*. Treatment of joint dysfunction in horses due to non-infectious synovitis associated with equine osteoarthritis.

(iii) *Limitations*. For intra-articular injection in horses only. Treatment may be repeated at weekly intervals for a total of four treatments. Not for use in horses intended for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(c)(1) *Specifications.* Each milliliter of sterile aqueous solution contains 10 milligrams of hyaluronate sodium.

(2) *Sponsor.* See 000856 in § 510.600(c) of this chapter.

(3) *Conditions of use—(i) Amount.* Small and medium-size joints (carpal, fetlock)—20 milligrams.

(ii) *Indications for use.* Treatment of carpal or fetlock joint dysfunction in horses due to acute or chronic noninfectious synovitis associated with equine osteoarthritis.

(iii) *Limitations.* For intraarticular injection in horses only. Treatment may be repeated after 1 or more weeks but not to exceed 2 injections per week for a total of 4 weeks. Not for use in horses intended for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(d)(1) *Specifications.* Each milliliter of sterile aqueous solution contains 10 milligrams of hyaluronate sodium.

(2) *Sponsor.* See 047408 in § 510.600(c) of this chapter.

(3) *Conditions of use—(i) Amount.* 50 milligrams in carpal and fetlock joints.

(ii) *Indications for use.* For treatment of equine carpal and fetlock joint dysfunction caused by traumatic and/or degenerative joint disease of mild to moderate severity.

(iii) *Limitations.* For intraarticular injection in horses only. Not for use in horses intended for food. Not intended for use in breeding animals. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[49 FR 45124, Nov. 15, 1984, as amended at 51 FR 11438, Apr. 3, 1986; 51 FR 25032, July 10, 1986; 53 FR 18773, May 31, 1988; 53 FR 22297, June 15, 1988]

§ 522.1150 Hydrochlorothiazide injection.

(a) *Specifications.* Each milliliter contains 25 milligrams of hydrochlorothiazide.

(b) *Sponsor.* See No. 000006 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* 5 to 10 milliliters (125 to 250 milligrams) intravenously or intramuscularly once or twice a day. After onset of diuresis, treatment may be continued with an orally administered maintenance dose.

(2) *Indications for use.* For use in cattle as an aid in the treatment of postparturient udder edema.¹

(3) *Limitations.* Animals should be regularly and carefully observed for early signs of fluid and electrolyte imbalance. Take appropriate countermeasures if this should occur. Milk taken from dairy animals during treatment and for 72 hours (6 milkings) after the latest treatment must not be used for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

[43 FR 59058, Dec. 19, 1978]

§ 522.1155 Imidocarb dipropionate sterile powder.

(a) *Specifications.* Imidocarb dipropionate powder is reconstituted with sterile water. Each milliliter of solution contains 100 milligrams of imidocarb base.

(b) *Sponsor.* No. 017220 in § 510.600(c) of this chapter.

(c) *Conditions of use.* The drug is used in horses and zebras as follows:

(1) *Amount.* For *Babesia caballi* infections, use intramuscularly 2 milligrams of imidocarb base per kilogram of body weight, repeating dosage once after 24 hours. For *Babesia equi* infections, use 4 milligrams of imidocarb base per kilogram of body weight, repeating dosage four times at 72-hour intervals.

(2) *Indications for use.* For the treatment of babesiosis (piroplasmosis) caused by *Babesia caballi* and *Babesia equi*.

(3) *Limitations.* Administer intramuscularly in the neck region. Do not inject intravenously. Do not use for other equidae or for animals of other species. Do not use in horses less than 1 year old. Do not use for animals in near-term pregnancies. Imidocarb dipropionate is a cholinesterase inhibitor. Do not use this product simultaneously with or a few days before or after treatment with or exposure to

¹ These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

cholinesterase-inhibiting drugs, pesticides, or chemicals. Do not use in horses intended for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian. Imidocarb dipropionate is sold only under permit issued by the Director of the National Program Planning Staff, Veterinary Services, APHIS, USDA, to licensed or full-time State, Federal, or military veterinarians.

[43 FR 40455, Sept. 12, 1978, as amended at 46 FR 48642, Oct. 2, 1981]

§ 522.1182 Iron dextran complex injection.

(a)(1) *Specifications.* Each milliliter of sterile solution contains ferric hydroxide dextran complex equivalent to 100 milligrams of elemental iron. It contains 0.5 percent phenol as a preservative.

(2)(i) *Sponsor.* See No. 010271 in § 510.600(c) of this chapter.

(ii) *Conditions of use.* It is used in baby pigs as follows:

(a) For the prevention of anemia due to iron deficiency, administer an initial intramuscular injection of 75 to 150 milligrams of elemental iron to each animal at 2 to 4 days of age. Dosage may be repeated in 14 to 21 days.

(b) For the treatment of anemia due to iron deficiency, administer an intramuscular injection of 100 to 200 milligrams of elemental iron.

(3)(i) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(ii) *Conditions of use.* It is used in baby pigs as follows:

(a) For the prevention of anemia due to iron deficiency, administer an initial intramuscular injection of 100 milligrams of elemental iron to each animal at 2 to 4 days of age. Dosage may be repeated in 14 to 21 days.

(b) For the treatment of anemia due to iron deficiency, administer an intramuscular injection of 200 milligrams of elemental iron.

(4)(i) *Sponsor.* See Nos. 000061 and 012525 in § 510.600(c) of this chapter.

(ii) *Conditions of use.* It is used in baby pigs as follows:

(a) For the prevention of iron deficiency anemia, administer intramuscularly an amount of drug containing 100 to 150 milligrams of elemental iron to animals from 1 to 3 days of age.

(b) For the treatment of iron deficiency anemia, administer intramuscularly an amount of drug containing 100 to 200 milligrams of elemental iron per animal. Dosage may be repeated in 10 days to 2 weeks.

(b)(1) *Specifications.* Each milliliter of sterile solution contains ferric hydroxide in complex with dextran equivalent to 200 milligrams of elemental iron. It contains 0.5 percent phenol as a preservative.

(2)(i) *Sponsor.* See No. 054273 in § 510.600(c) of this chapter.

(ii) *Conditions of use.* It is used in baby pigs as follows:

(a) For prevention of baby pig anemia due to iron deficiency, intramuscularly inject 200 milligrams of elemental iron (1 milliliter) at 1 to 3 days of age.

(b) For treatment of baby pig anemia due to iron deficiency, intramuscularly inject 200 milligrams of elemental iron at the first sign of anemia.

[49 FR 38938, Oct. 2, 1984, as amended 53 FR 7832, Mar. 13, 1987; 53 FR 40727, Oct. 18, 1988]

§ 522.1183 Iron hydrogenated dextran injection.

(a) *Specifications.* Each milliliter contains 100 milligrams of elemental iron stabilized with a low molecular weight hydrogenated dextran and 0.5 percent phenol as a preservative.

(b) *NAS/NRC status.* Use of this drug has been NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(c)(1) *Sponsor.* See No. 000986 in § 510.600(c) of this chapter.

(2) *Conditions of use.* It is used in baby pigs as follows:

(i) For the prevention of anemia due to iron deficiency, administer an initial intramuscular injection of 100 milligrams of elemental iron to each animal at 2 to 5 days of age. Dosage may be repeated at 2 weeks of age.

(ii) For the treatment of anemia due to iron deficiency, administer an intramuscular injection of 100 milligrams of elemental iron to each animal when

indicated between 5 and 28 days of age.

(d)(1) *Sponsor*. See No. 000003 in § 510.600(c) of this chapter.

(2) *Conditions of use*. It is used in baby pigs as follows:

(i) For the prevention of anemia due to iron deficiency, administer by intramuscular or subcutaneous injection of 100 milligrams of elemental iron to each animal at 2 to 4 days of age.

(ii) For the treatment of anemia due to iron deficiency, administer by intramuscular or subcutaneous injection of 100 milligrams of elemental iron in baby pigs up to 4 weeks of age.

(e)(1) *Sponsors*. See Nos. 017287, 053617, and 054273 in § 510.600(c) of this chapter.

(2) *Conditions of use*. It is used in baby pigs as follows:

(i) For the prevention of iron deficiency anemia, administer intramuscularly 100 milligrams at 2 to 4 days of age.

(ii) For the treatment of iron deficiency anemia, administer intramuscularly 100 milligrams. Treatment may be repeated in 10 days.

(f)(1) *Sponsor*. See No. 000010 in § 510.600(c) of this chapter.

(2) *Conditions of use*. It is used in baby pigs as follows:

(i) For prevention of iron deficiency anemia, administer intramuscularly 100 milligrams at 2 to 4 days of age. Dosage may be repeated at 14 to 21 days.

(ii) For treatment of iron deficiency anemia, administer intramuscularly 100 to 200 milligrams when indicated between 5 to 28 days of age.

142 FR 53955, Oct. 4, 1977, as amended at 46 FR 39128, July 31, 1981; 50 FR 23298, June 3, 1985; 52 FR 18691, May 19, 1987; 52 FR 36023, Sept. 25, 1987; 53 FR 40728 and 40729, Oct. 18, 1988]

§ 522.1192 Ivermectin injection.

(a) *Specifications*—(1) *Horses*. Each milliliter of sterile aqueous solution contains 20 milligrams of ivermectin (2 percent).

(2) *Cattle, reindeer, and swine*. Each milliliter of sterile aqueous solution contains 10 milligrams of ivermectin (1 percent).

(3) *Piglets 70 pounds or less*. Each milliliter of sterile aqueous solution

contains 2.7 milligrams of ivermectin (0.27 percent).

(b) *Sponsor*. See No. 000006 in § 510.600(c) of this chapter.

(c) *Related tolerances*. See § 556.344 of this chapter.

(d) *Conditions of use*—(1) *Horses*—(i) *Amount*. 20 milligrams per 100 kilograms (220 pounds) of body weight.

(ii) *Indications for use*. It is used in horses for the treatment and control of large strongyles (adult) (*Strongylus vulgaris*, *Strongylus edentatus*, *Triodontophorus* spp.), small strongyles (adult and fourth stage larvae) (*Cyathostomum* spp., *Cylicocyclus* spp., *Cylicostephanus* spp.), pinworms (adult and fourth-stage larvae) (*Oxyuris equi*), large roundworms (adult) (*Parascaris equorum*), hairworms (adult) (*Trichostrongylus axei*), large mouth stomach worms (adult) (*Habronema muscae*), neck threadworms (*microfilariae*) (*Onchocerca* spp.), and stomach bots (*Gastrophilus* spp.).

(iii) *Limitations*. For intramuscular use only. Do not use intravenously. Not for use in horses intended for food. Effects of this drug on pregnant mares have not been determined. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(2) *Cattle*—(i) *Amount*. 10 milligrams per 50 kilograms (110 pounds) body weight (200 micrograms per kilogram).

(ii) *Indications for use*. It is used in cattle for the treatment and control of gastrointestinal nematodes (adults and fourth-stage larvae) (*Haemonchus placei*, *Ostertagia ostertagi* (including inhibited larvae), *O. lyrata*, *Trichostrongylus axei*, *T. colubriformis*, *Coo-peria oncophora*, *C. punctata*, *C. pectinata*, *Oesophagostomum radiatum*, *Nematodirus helvetianus* (adults only), *N. spathiger* (adults only), *Bunostomum phlebotomum*); lungworms (adults and fourth-stage larvae) (*Dic-tyocaulus viviparus*); grubs (first, second, and third instars) (*Hypoderma bovis*, *H. lineatum*); lice (*Linognathus vituli*, *Haematopinus eurysternus*, *Solenopotes capillatus*); mites (*Psoroptes ovis* (syn. *P. communis* var. *bovis*), *Sarcoptes scabiei* var. *bovis*).

(iii) *Limitations*. For subcutaneous use only. Not for intramuscular use. Do not treat cattle within 35 days of slaughter. Because a withdrawal time

in milk has not been established, do not use in female dairy cattle of breeding age. Do not use in other animal species because severe adverse reactions, including fatalities in dogs, may result. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

(3) *Reindeer*—(i) *Amount*. 10 milligrams per 50 kilograms (110 pounds) body weight.

(ii) *Indications for use*. It is used in reindeer for treatment and control of warbles (*Oedemagena tarandi*).

(iii) *Limitations*. For subcutaneous use only. Not for intramuscular use. Do not treat reindeer within 56 days of slaughter. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(4) *Swine*—

(i) *Amount*. 10 milligrams per 75 pounds of body weight.

(ii) *Indications for use*. It is used in swine for treatment and control of gastrointestinal nematodes (adults and fourth-stage larvae) (*Ascaris suum*, *Hyostrogylus rubidus*, *Oesophagostomum* spp., *Strongyloides ransomi* (adults only)); lungworms (*Metastrongylus* spp. (adults only)); lice (*Haematopinus suis*); and mites (*Sarcoptes scabiei* var. *suis*).

(iii) *Limitations*. For subcutaneous injection in the neck of swine only. Do not treat swine within 18 days of slaughter. Do not use in other animal species as severe adverse reactions, including fatalities in dogs, may result. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

[49 FR 5344, Feb. 13, 1984, as amended at 50 FR 30266, July 25, 1985; 51 FR 25686, July 16, 1986; 51 FR 27021, July 29, 1986; 51 FR 29463, Aug. 18, 1986; 53 FR 11064, Apr. 5, 1988]

§ 522.1204 Kanamycin sulfate injection.

(a) *Specifications*. Kanamycin sulfate injection veterinary conforms to the standards of identity, strength, quality, and purity prescribed by § 444.230(a) of this chapter, except that each milliliter contains either 50 or 200 milligrams of kanamycin.

(b) *Sponsor*. See No. 000856 in § 510.600(c) of this chapter.

(c) *Conditions of use*. (1) It is used for the treatment of bacterial infection due to kanamycin sensitive organisms in dogs and cats.

(2) It is administered subcutaneously or intramuscularly at 5 milligrams per pound of body weight per day in equally divided doses at 12-hour intervals.

(3) Its label shall bear an appropriate expiration date.

(4) Restricted to use by or on the order of a licensed veterinarian.

[40 FR 13858, Mar. 27, 1975, as amended at 53 FR 27851, July 25, 1988]

§ 522.1222 Ketamine hydrochloride injectable dosage forms.

§ 522.1222a Ketamine hydrochloride injection.

(a) *Chemical name*. 2-(o-Chlorophenyl)-2-(methylamino) cyclohexanone hydrochloride.

(b) *Specifications*. The drug is a sterile aqueous solution and each milliliter contains: Ketamine hydrochloride equivalent to 100 milligrams ketamine base activity and 1:10,000 benzethonium chloride.

(c) *Sponsors*. (1) See No. 000856 in § 510.600(c) of this chapter.

(2) See No. 000856 in § 510.600(c) of this chapter.

(d) *Special considerations*. Store in a cool place. Protect from light. Do not use if precipitate appears.

(e) *Conditions of use*. (1) In cats: (i) It is used for restraint or as the sole anesthetic agent in diagnostic or minor, brief surgical procedures that do not require skeletal muscle relaxation.

(ii) It is administered intramuscularly at a recommended dose that ranges from 5 to 15 milligrams per pound of body weight depending on the effect desired.

(2) In subhuman primates: (i) It is used for restraint.

(ii) It is administered intramuscularly at a recommended dose that ranges from 3 to 15 milligrams per kilogram of body weight depending upon the species, general condition, and age of the subject.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 59342, Dec. 23, 1975, as amended at 53 FR 23390, June 22, 1988; 53 FR 27851, July 25, 1988]

§ 522.1222b Ketamine hydrochloride with promazine hydrochloride and aminopentamide hydrogen sulfate injection.

(a) *Chemical name.* Ketamine hydrochloride, (±), 2-(o-chlorophenyl)-2-(methylamino) cyclohexanone hydrochloride, with promazine hydrochloride, 10-(3-(dimethylamino) propyl) phenothiazine monohydrochloride, and aminopentamide hydrogen sulfate.

(b) *Specifications.* The drug is a sterile aqueous solution and each milliliter contains: Ketamine hydrochloride equivalent to 100 milligrams ketamine base activity, 7.5 milligrams of promazine hydrochloride, and 0.0625 milligram of aminopentamide hydrogen sulfate, with 1:10,000 benzethonium chloride.

(c) *Sponsor.* See Code No. 000856 in § 510.600(c) of this chapter.

(d) *Special considerations.* Store in a cool place. Protect from light. Do not use if precipitate appears.

(e) *Conditions of use.* (1) It is used in cats as the sole anesthetic agent for ovariohysterectomy and general surgery.

(2) It is administered intramuscularly at a recommended dose from 15 to 20 milligrams ketamine base per pound of body weight, depending on the effect desired.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 59342, Dec. 23, 1975, as amended at 42 FR 3838, Jan. 21, 1977; 53 FR 27851, July 25, 1988]

§ 522.1228 Lactic acid.

(a) *Chemical name.* 2-Hydroxy-propanoic acid.

(b) *Specifications.* Each milliliter of sterile solution contains 1.200 grams of lactic acid. Conforms to lactic acid U.S.P.

(c) *Sponsor.* See No. 000010 in § 510.600(c) of this chapter.

(d) *Conditions of use—(1) Indications for use.* It is used to castrate bull calves up to 150 pounds.

(2) *Amount.* As a single injection at 1 milliliter per testis for bulls up to 100 pounds and at 1.5 milliliters per testis for bulls weighing 101 to 150 pounds.

(3) *Limitations.* It is administered intratesticular. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[48 FR 34948, Aug. 2, 1983]

§ 522.1235 Lenperone hydrochloride injection.

(a) *Specifications.* Each milliliter of sterile solution contains 5 milligrams of lenperone hydrochloride.

(b) *Sponsor.* See No. 000031 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) Used in cats and dogs as a tranquilizer, antiemetic, and for pre- and postoperative medication.

(2) Administered intravenously at .10 to .40 milligram per pound of body weight; intramuscularly at .20 to .80 milligram per pound of body weight, but not more than 4 milliliters per injection site.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[46 FR 25086, May 5, 1981]

§ 522.1244 Levamisole phosphate injection.

(a) *Specifications.* Each milliliter of sterile aqueous solution contains levamisole phosphate equivalent to 136.5 or 182 milligrams of levamisole hydrochloride (13.65 or 18.2 percent).

(b) *Sponsor.* See No. 011716 in § 510.600 of this chapter for use of 13.65 percent injection, and see No. 043781 for use of 13.65 and 18.2 percent injection.

(c) *Conditions of use—(1) Amount.* 2 milliliters per 100 pounds of body weight, subcutaneously in the neck.

(2) *Indications for use.* (1) The 13.65 percent injection is used as an anthelmintic in cattle for treatment of the following parasites: stomach worms (*Haemonchus*, *Trichostrongylus*, *Ostertagia*), intestinal worms (*Trichostrongylus*, *Cooperia*, *Nematodirus*,

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Bunostomum, *Oesophagostomum*, *Chabertia*), and lungworms (*Dictyocaulus*).

(ii) The 18.2 percent injection is used as an anthelmintic in cattle for treatment of the following parasites: stomach worms (*Haemonchus*, *Trichostrongylus*, *Ostertagia*), intestinal worms (*Trichostrongylus*, *Cooperia*, *Nematodirus*, *Bunostomum*, *Oesophagostomum*) and lungworms (*Dictyocaulus*).

(3) *Limitations*. Do not administer more than 10 milliliters per site. Cattle that are severely parasitized or maintained under conditions of constant helminth exposure may require re-treatment within 2 to 4 weeks after first treatment. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism. Consult your veterinarian before using in severely debilitated animals or animals under severe stress. Do not administer to cattle within 7 days of slaughter. Do not administer to dairy animals of breeding age.

[43 FR 20489, May 12, 1978, as amended at 43 FR 29289, July 7, 1978; 43 FR 60895, Dec. 29, 1978; 47 FR 10807, Mar. 12, 1982]

§ 522.1258 Lidocaine injection with epinephrine.

(a) *Specifications*. Each milliliter of the drug contains 20 milligrams (2 percent) of lidocaine hydrochloride, 0.01 milligram of epinephrine, with sodium chloride, and with methylparaben as a preservative, in water for injection.

(b) *Sponsor*. See No. 000402 in § 510.600(c) of this chapter.

(c) *Conditions of use*¹—(1) *Amount*. The drug is administered by injection as a 2 percent solution or diluted with bacteriostatic water for injection to a 0.5 percent solution for local anesthesia of large and small animals, as follows:

(i) Cats: Administer approximately 2 milliliters of 2 percent solution with epinephrine by caudal injection.

¹These conditions are National Academy of Science/National Research Council reviewed and deemed effective for this drug. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter but may require bioequivalency and safety information.

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(ii) Cattle: Administer 5 milliliters of 2 percent solution with epinephrine by epidural injection (standing animal). Administer 10 to 20 milliliters of 2 percent solution with epinephrine by cornual nerve block injection. For teat operations and infiltration, inject 0.5 percent solution with epinephrine to effect.

(iii) Dogs: Administer 2 to 10 milliliters of 2 percent solution with epinephrine by caudal injection. Do not give intravascularly. For infiltration, administer 0.5 percent solution with epinephrine to effect.

(iv) Horses: Administer 5 to 10 milliliters of 2 percent solution with epinephrine by volar nerve block. Administer 10 to 15 milliliters of 2 percent solution with epinephrine by epidural injection. For standing animal, apply slowly and observe individual sensitivity. For infiltration, administer 0.5 percent solution with epinephrine to effect.

(2) *Limitations*. (i) The drug is contraindicated in the presence of sepsis in the region of proposed injection, shock and heart block, neurologic disease, spinal deformities, septicemia, and hypertension.

(ii) Do not give intravascularly.

(iii) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[43 FR 46300, Oct. 6, 1978; 43 FR 59059, Dec. 19, 1978, as amended at 52 FR 25212, July 3, 1987]

§ 522.1260 Lincomycin injection.

(a) *Specifications*. Each milliliter of sterile aqueous solution contains lincomycin hydrochloride equivalent to 25, 50, 100, or 300 milligrams of lincomycin.

(b) *Sponsor*. See No. 000009 in § 510.600(c) of this chapter.

(c) *Special considerations*. When common labeling for use of the drug in dogs, cats, and swine is included with the drug, all such uses are subject to the labeling requirements of § 201.105 of this chapter.

(d) *Related tolerances*. See § 556.360 of this chapter.

(e) *Conditions of use*. It is used for animals as follows:

(1) *Dogs and cats*—(i) *Amount*. 5 to 10 milligrams per pound of body weight per day.

(ii) *Indications for use*. Infections caused by Gram-positive organisms, particularly streptococci and staphylococci.

(iii) *Limitations*. Administer intramuscularly 10 milligrams per pound of body weight once a day or 5 milligrams per pound of body weight twice daily or intravenously 5 to 10 milligrams per pound of body weight one or two times daily by slow injection. May be diluted with 5 percent glucose in water or normal saline and given as an infusion; as lincomycin hydrochloride monohydrate; for use by or on the order of a licensed veterinarian.

(2) *Swine*—(i) *Amount*. 5 milligrams per pound of body weight per day.

(ii) *Indications for use*. Treatment of infectious arthritis and mycoplasma pneumonia.

(iii) *Limitations*. Administer intramuscularly as a single daily dose for 3 to 7 days; as lincomycin hydrochloride monohydrate; do not treat within 48 hours of slaughter.

[40 FR 13858, Mar. 27, 1975, as amended at 50 FR 31351, Aug. 2, 1985]

§ 522.1372 Mepivacaine hydrochloride injection.

(a) *Specifications*. Each milliliter of sterile aqueous solution contains 20 milligrams of mepivacaine hydrochloride.

(b) *Sponsor*. See No. 000934 in § 510.600(c) of this chapter.

(c) *Conditions of use*. (1) It is intended for use in horses as a local anesthetic for infiltration, nerve block, intra-articular and epidural anesthesia and topical and/or infiltration anesthesia of the laryngeal mucosa prior to ventriculectomy.

(2) It is administered as follows: for nerve block, 3 to 15 milliliters; for epidural anesthesia, 5 to 20 milliliters; for intra-articular anesthesia, 10 to 15 milliliters; for infiltration, as required; for anesthesia of the laryngeal mucosa prior to ventriculectomy, by topical spray, 25 to 40 milliliters, by infiltration, 20 to 50 milliliters.

(3) Not for use in horses intended for food.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[42 FR 5349, Jan. 28, 1977, as amended at 42 FR 36995, July 19, 1977]

§ 522.1380 Methocarbamol injection.

(a) *Specifications*. The product is a sterile, pyrogen-free solution, each milliliter containing 100 milligrams of methocarbamol, 0.5 milliliter of polyethylene glycol 300, and water for injection q.s. Its pH is 3.5 to 6.0.

(b) *Sponsor*. See 000031 in § 510.600(c) of this chapter.

(c) *Conditions of use*—(1) *Amount*—

(i) *Dogs and cats*. 20 milligrams per pound of body weight for moderate conditions, 25 to 100 milligrams per pound of body weight for severe conditions (tetanus and strychnine poisoning), total cumulative dose not to exceed 150 milligrams per pound of body weight.

(ii) *Horses*. 2 to 10 milligrams per pound of body weight for moderate conditions, 10 to 25 milligrams per pound of body weight for severe conditions (tetanus), additional amounts may be needed to relieve residual effects and to prevent recurrence of symptoms.

(2) *Indications for use*. As an adjunct for treating acute inflammatory and traumatic conditions of the skeletal muscles and to reduce muscular spasms.

(3) *Limitations*. For intravenous use only. For dogs, administer rapidly half the estimated dose, pause until the animal starts to relax, then continue administration to effect. For horses, administer rapidly to effect. Not for horses intended for food use. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[45 FR 79758, Dec. 2, 1980, as amended at 46 FR 18964, Mar. 27, 1981]

§ 522.1410 Sterile methylprednisolone acetate suspension.

(a) *Specifications*. Each milliliter of aqueous suspension contains 20 or 40

milligrams of methylprednisolone acetate.¹

(b) *Sponsors.* See Nos. 000009 and 054273 in § 510.600(c) of this chapter.

(c) *Special considerations.* (1) Clinical and experimental data have demonstrated that corticosteroids administered orally or parenterally to animals may induce the first stage of parturition when administered during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis.

(2) *Systemic therapy with methylprednisolone acetate,* as with other corticoids, is contraindicated in animals with arrested tuberculosis, peptic ulcer, and Cushing's syndrome. The presence of active tuberculosis, diabetes mellitus, osteoporosis, renal insufficiency, predisposition to thrombophlebitis, hypertension, or congestive heart failure necessitates carefully controlled use of corticosteroids. Intra-synovial, intratendinous, or other injections of corticosteroids for local effect are contraindicated in the presence of acute infectious conditions. Exacerbation of pain, further loss of joint motion, with fever and malaise following injection may indicate that the condition has become septic. Appropriate antibacterial therapy should be instituted immediately.

(d) *Conditions of use—(1) Amount—*

(i) *Intramuscular.* Dosage may be repeated when necessary, as follows: dogs—2 to 40 milligrams (up to 120 milligrams in extremely large breeds or dogs with severe involvement); cats—10 to 20 milligrams; horses—200 milligrams.¹

(ii) *Intrasynovial.* Dosage may be repeated when necessary, as follows: horses—40 to 240 milligrams; dogs—up to 20 milligrams.¹

¹ These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

¹ These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter but may require bioequivalency and safety information.

(2) *Indications for use.* Treatment of inflammation and related disorders in dogs, cats, and horses;¹ treatment of allergic and dermatologic disorders in dogs and cats; and as supportive therapy to antibacterial treatment of severe infections in dogs and cats.

(3) *Limitations.* Not for use in horses intended for food. Not for human use. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[43 FR 59058, Dec. 19, 1978, as amended at 51 FR 741, Jan. 8, 1986; 53 FR 40728, Oct. 18, 1988]

§ 522.1452 Nalorphine hydrochloride injection.

(a) *Specifications.* Each milliliter of aqueous solution contains 5 milligrams of nalorphine hydrochloride.

(b) *Sponsor.* See No. 000006 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* One milligram per 5 pounds; intravenously, intramuscularly, or subcutaneously.

(2) *Indications for use.* Respiratory and circulatory depression in dogs resulting from overdosage of, or unusual sensitivity to, morphine and certain other narcotics. Not for depression due to any other cause.

(3) *Limitations.* Successive doses of the drug gradually lose their analeptic effect and eventually induce respiratory depression equal to that of opiates. Therefore, do not exceed therapeutic dosage. Do not mix drug with meperidine solutions because the buffer will cause precipitation. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[44 FR 6707, Feb. 2, 1979, as amended at 47 FR 36418, Aug. 20, 1982]

§ 522.1462 Naloxone hydrochloride injection.

(a) *Specifications.* Naloxone hydrochloride injection is an aqueous sterile solution containing 0.4 milligram of naloxone hydrochloride per milliliter.

(b) *Sponsor.* See No. 000590 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is used as a narcotic antagonist in dogs.

(2) It is administered by intravenous, intramuscular, or subcutaneous injection.

tion at an initial dose of 0.04 milligram per kilogram of body weight. When given intravenously, the dosage may be repeated at 2- to 3-minute intervals as necessary. Onset of action by intramuscular or subcutaneous injection is slightly longer than it is by intravenous injection, and repeated dosages must be administered accordingly.

(3) For use only by or on the order of a licensed veterinarian.

[40 FR 13858, Mar. 27, 1975, as amended at 47 FR 20757, May 14, 1982]

§ 522.1468 Naproxen for injection.

(a) *Specifications.* The drug is a lyophilized powder which is reconstituted with sterile water for injection to form a 10 percent sterile aqueous solution (100 milligrams per milliliter).

(b) *Sponsor.* See 000033 in § 510.600(c) of this chapter.

(c) *Conditions of use in horses.* (1) *Dosage.* Five milligrams per kilogram of body weight intravenously followed by maintenance oral therapy of 10 milligrams per kilogram of body weight twice daily for up to 14 consecutive days.

(2) *Indications for use.* For the relief of inflammation and associated pain and lameness exhibited with arthritis, as well as myositis and other soft tissue diseases of the musculoskeletal system of the horse.

(3) *Limitations.* Not for use in horses intended for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[46 FR 26763, May 15, 1981. Redesignated and amended at 51 FR 24525, July 7, 1986]

§ 522.1484 Neomycin sulfate sterile solution.

(a) *Specifications.* Each milliliter of sterile aqueous solution contains 50 milligrams of neomycin sulfate (equivalent to 35 milligrams of neomycin base). The neomycin sulfate used in manufacturing the drug conforms to the standards of identity, strength, quality, and purity prescribed by § 444.42a(a)(1) of this chapter.¹

¹These claims are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter.

(b) *Sponsor.* See No. 000009 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) *Amount.* 5 milligrams per pound of body weight daily divided into portions administered every 6 to 8 hours for 3 to 5 days.¹

(2) *Indications for use.* Administer to dogs and cats for the treatment of acute and chronic bacterial infections due to organisms susceptible to neomycin.¹

(3) *Limitations.* For intramuscular or intravenous use only. Neomycin is not for use parenterally in food-producing animals because of prolonged residues in edible tissues. Labeling shall bear an appropriate expiration date. For use by or on the order of a licensed veterinarian.¹

[43 FR 48996, Oct. 20, 1978]

§ 522.1503 Neostigmine methylsulfate injection.

(a) *Specifications.* Neostigmine methylsulfate injection contains two milligrams of neostigmine methylsulfate in each milliliter of sterile aqueous solution.

(b) *Sponsor.* See No. 011716 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is intended for use for treating rumen atony; initiating peristalsis which causes evacuation of the bowel; emptying the urinary bladder; and stimulating skeletal muscle contractions. It is a curare antagonist.

(2) It is administered to cattle and horses at a dosage level of 1 milligram per 100 pounds of body weight subcutaneously. It is administered to sheep at a dosage level of 1 to 1½ milligrams per 100 pounds body weight subcutaneously. It is administered to swine at a dosage level of 2 to 3 milligrams per 100 pounds body weight intramuscularly. These doses may be repeated as indicated.

(3) The drug is contraindicated in mechanical, intestinal or urinary obstruction, late pregnancy, and in animals treated with other cholinesterase inhibitors.

(4) Not for use in animals producing milk, since this use will result in contamination of the milk.

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(5) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

§ 522.1563 Nitrofurantoin sodium injection.

(a) *Specifications.* It is sterile and packaged so that each vial contains sufficient drug to permit withdrawal of 180 milligrams of nitrofurantoin sodium. The nitrofurantoin sodium used is the sodium salt of nitrofurantoin U.S.P.

(b) *Sponsor.* See No. 000149 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is used only in bacterial infections of the urinary tract of dogs when the oral forms are not feasible.

(2) It is administered intramuscularly at the rate of 1.5 milligrams of nitrofurantoin sodium per pound of body weight twice daily (total daily dose: 3 milligrams per pound) for a maximum of 10 days.

(3) For use by or on the order of a licensed veterinarian.

[40 FR 13858, Mar. 27, 1975, as amended at 44 FR 67114, Nov. 23, 1979]

§ 522.1610 Oleate sodium solution.

(a) *Specifications.* Each milliliter of sterile aqueous solution contains 50 milligrams of sodium oleate.

(b) *Sponsor.* See No. 037990 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is used in horses to stimulate infiltration of cellular blood components that subsequently differentiate into fibrous and/or fibrocartilagenous tissue.

(2) The drug is administered by parenteral injection dependent upon the area of response desired. An injection of 1 milliliter will produce a response of approximately 15 square centimeters. Do not inject more than 2 milliliters per injection site. Regardless of the number of injection sites, the total volume used should not exceed 10 milliliters.

(3) Not for use in horses intended for food.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[41 FR 27034, July 1, 1976, as amended at 50 FR 40966, Oct. 8, 1985]

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§ 522.1620 Orgotein for injection.

(a) *Specifications.* Orgotein for injection is packaged in a vial containing 5 milligrams of orgotein and 10 milligrams of sucrose as lyophilized sterile nonpyrogenic powder with directions for dissolving the contents of the vial in 2 milliliters of diluent which is sodium chloride injection, U.S.P.

(b) *Sponsor.* See No. 024991 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) *Horses.* (i) It is used in the treatment of soft tissue inflammation associated with the musculoskeletal system.

(ii) It is administered by deep intramuscular injection at a dosage level of 5 milligrams every other day for 2 weeks and twice weekly for 2 to 3 more weeks. Severe cases, both acute and chronic, may benefit more from daily therapy initially. Dosage may be continued beyond 5 weeks if satisfactory improvement has not been achieved.

(iii) Not for use in horses intended for food.

(2) *Dogs.* (i) It is used for the relief of inflammation associated with ankylosing spondylitis, spondylosis, and disc disease. When severe nerve damage is present, response will occur much more slowly, if at all.

(ii) It is administered by subcutaneous injection at a dosage level of 5 milligrams every day for 6 days, and thereafter, every other day for 8 days. In less severe conditions, shorter courses of therapy may be indicated.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13858, Mar. 27, 1975, as amended at 41 FR 32583, Aug. 4, 1976]

§ 522.1642 Oxymorphone hydrochloride injection.

(a) *Specifications.* The drug contains 1 or 1.5 milligrams of oxymorphone hydrochloride per milliliter of aqueous solution containing 0.8 percent sodium chloride.

(b) *Sponsor.* See No. 900056 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is a narcotic analgesic, preanesthetic, anesthetic, and substitute anesthetic adjuvant for intramuscular, subcutane-

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ous or intravenous administration to cats and dogs as follows:

Animal	Body weight (pounds)	Dosage (milligram)
Dogs	2 to 5	0.75
	5 to 15	0.75-1.5
	15 to 30	1.5-2.5
	30 to 60	2.5-4.0
	Over 60	4.0
Cats	Small	0.4-0.75
	Large	0.75-1.5

(2) Do not mix with a barbiturate in the same syringe to preclude precipitation.

(3) It tends to depress respiration. Naloxone hydrochloride and other narcotic antagonists are used to counter over-dosing.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

§ 522.1660 Oxytetracycline injection.

(a) *Specifications.* Each milliliter of sterile solution contains 200 milligrams of oxytetracycline base.

(b) *Sponsor.* See 000069 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1)—Beef cattle and nonlactating dairy cattle—*

(i) *Amount.* 3 to 5 milligrams of oxytetracycline per pound of body weight per day; 5 milligrams per pound of body weight per day for treatment of anaplasmosis, severe foot-rot, and advanced cases of other indicated diseases; 9 milligrams per pound of body weight as a single dosage where re-treatment for anaplasmosis is impractical; 9 milligrams per pound of body weight as single dosage where retreatment of calves and yearlings for bacterial pneumonia is impractical; 9 milligrams per pound of body weight as a single dosage for treatment of infectious bovine keratoconjunctivitis.

(ii) *Indications for use.* Treatment of diseases due to oxytetracycline-susceptible organisms as follows: Pneumonia and shipping fever complex associated with *Pasteurella* spp. and *Hemophilus* spp., foot-rot and diphtheria caused by *Fusobacterium necrophorum*, bacterial enteritis (scours) caused by *Escherichia coli*, wooden tongue caused by *Actinobacillus lignieresii*, leptospirosis caused by *Lepto-*

spira pomona, wound infections and acute metritis caused by *staphylococcus* spp. and *Streptococcus* spp., and infectious bovine keratoconjunctivitis (pinkeye) caused by *Moraxella bovis*. If labeled for use by or on the order of a licensed veterinarian, it may also be used for treatment of anaplasmosis caused by *Anaplasma marginale* and anthrax caused by *Bacillus anthracis*.

(iii) *Limitations.* Administer intramuscularly or intravenously at 3 to 5 milligrams level; intramuscularly only at 9 milligrams level. Treatment of all diseases should be instituted early and continued for 24 to 48 hours beyond remission of disease symptoms, but not to exceed a total of 4 consecutive days. Consult your veterinarian if no improvement is noted within 48 hours. Do not inject more than 10 milliliters per site in adult cattle, reducing the volume according to age and body size to 1 to 2 milliliters in small calves. Exceeding the highest recommended dose, administering at recommended levels for more than 4 consecutive days, and/or exceeding 10 milliliters intramuscularly per injection site may result in antibiotic residues beyond the withdrawal time. Discontinue treatment at least 28 days prior to slaughter. Not for use in lactating dairy cattle.

(2) *Swine—(i) Amount.* 3 to 5 milligrams of oxytetracycline per pound of body weight per day; 9 milligrams per pound of body weight as a single dosage where re-treatment for pneumonia is impractical. Sows: Administer once 3 milligrams of oxytetracycline per pound of body weight, approximately 8 hours before farrowing or immediately after completion of farrowing.

(ii) *Indications for use.* Treatment of bacterial enteritis (scours, colibacillosis) caused by *Escherichia coli*, pneumonia caused by *Pasteurella multocida*, and leptospirosis caused by *Leptospira pomona*. Sows: as an aid in control of infectious enteritis (baby pig scours, colibacillosis) in suckling pigs caused by *Escherichia coli*.

(iii) *Limitations.* Administer intramuscularly. Do not inject more than 5 milliliters per site in adult swine. Discontinue treatment at least 28 days prior to slaughter.

§ 522.1662a

[45 FR 16479, Mar. 14, 1980, as amended at 46 FR 20160, Apr. 3, 1981; 46 FR 27913, May 22, 1981; 52 FR 19502, May 26, 1987]

§ 522.1662 Oxytetracycline hydrochloride implantation or injectable dosage forms.

§ 522.1662a Oxytetracycline hydrochloride injection.

(a)(1) *Specifications.* The drug contains 50 milligrams of oxytetracycline hydrochloride in each milliliter of sterile solution.

(2) *Sponsor.* See No. 054273 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) The drug is intended for use in beef cattle, beef calves, nonlactating dairy cattle, and dairy calves for treatment of disease conditions caused by one or more of the following oxytetracycline sensitive pathogens listed as follows: pneumonia and shipping fever complex (*Pasteurella* spp.; *Hemophilus* spp.; *Klebsiella* spp.), bacterial enteritis (scours) (*E. coli*), foot-rot (*Spherophorus necrophorus*), diphtheria (*Spherophorus necrophorus*), wooden tongue (*Actinobacillus lignieresii*), leptospirosis (*Leptospira pomona*), and wound infections; acute metritis; traumatic injury (caused by a variety of bacterial organisms (such as streptococcal and staphylococcal organisms).)

(ii) It is administered by intramuscular injection of 3 to 5 milligrams of oxytetracycline hydrochloride per pound of body weight per day. Leptospirosis, severe foot-rot and severe forms of the indicated diseases should be treated with 5 milligrams per pound of body weight per day. Treatment should be continued for 24 to 48 hours following remission of disease symptoms; however, not to exceed a total of 4 consecutive days. Only 2 milliliters of the drug should be injected per site in case of calves weighing 100 pounds or less and not more than 10 milliliters should be injected per site in adult cattle.

(iii) Discontinue treatment with the drug at least 20 days prior to slaughter of the animal. When administered to animals within 30 days of slaughter, muscle discoloration may necessitate trimming of injection site and surrounding tissues.

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(iv) For use only in beef cattle, beef calves, nonlactating dairy cattle, and dairy calves.

(b)(1) *Specifications.* Each milliliter of sterile solution contains 50 or 100 milligrams of oxytetracycline (as oxytetracycline hydrochloride).

(2) *Sponsor.* See 000010 in § 510.600(c) of this chapter.

(3) *Conditions of use.*—(i) *Beef cattle and nonlactating dairy cattle.*—(a) *Amount.* Three to 5 milligrams of oxytetracycline per pound of body weight per day; 5 milligrams per pound of body weight per day for the treatment of anaplasmosis, severe foot-rot, and severe cases of other indicated diseases.

(b) *Indications for use.* Treatment of diseases due to oxytetracycline-susceptible organisms as follows: Pneumonia and shipping fever complex associated with *Pasteurella* spp., *Hemophilus* spp., and *Klebsiella* spp., foot-rot and diphtheria caused by *Spherophorus necrophorus*, bacterial enteritis (scours) caused by *Escherichia coli*, wooden tongue caused by *Actinobacillus lignieresii*, leptospirosis caused by *Leptospira pomona*, and wound infections and acute metritis caused by *Staphylococcus* spp. and *Streptococcus* spp. If labeled for use by or on the order of a licensed veterinarian, it may be used for the treatment of anaplasmosis caused by *Anaplasma marginale*.

(c) *Limitations.* For 50-milligram-per-milliliter solution, administer intramuscularly or intravenously; for 100-milligram-per-milliliter solution, administer intramuscularly only. Treatment of all diseases should be instituted early and continue for 24 to 48 hours beyond remission of disease symptoms, but not to exceed a total of 4 consecutive days. Consult your veterinarian if no improvement is noted within 48 hours. Do not inject more than 10 milliliters per site in adult cattle, reducing the volume according to age and body size to 0.5 to 2 milliliters in small calves. Exceeding the highest recommended dose of 5 milligrams per pound of body weight, administering at recommended levels for more than 4 consecutive days, and/or exceeding 10 milliliters intramuscularly per injection site may result in antibiotic residues beyond the withdrawal

time. Discontinue treatment at least 18 days prior to slaughter. Not for use in lactating dairy cattle.

(ii) *Swine*—(a) *Amount*. Three to 5 milligrams of oxytetracycline per pound of body weight per day. Sows: 3 milligrams of oxytetracycline per pound of body weight, approximately 8 hours before farrowing or immediately after completion of farrowing.

(b) *Indications for use*. For treatment of bacterial enteritis (scours, colibacillosis) caused by *Escherichia coli*, pneumonia caused by *Pasteurella multocida*, and leptospirosis caused by *Leptospira pomona*. Sows: as an aid in control of infectious enteritis (baby pig scours, colibacillosis) in suckling pigs caused by *Escherichia coli*.

(c) *Limitations*. Administer intramuscularly. Do not inject more than 5 milliliters per site. Do not use for more than 4 consecutive days. Discontinue treatment at least 26 days before slaughter.

(c)(1) *Specifications*. The drug contains 50 or 100 milligrams of oxytetracycline hydrochloride in each milliliter of sterile solution.

(2) *Sponsor*. See No. 000069 in § 510.600(c) of this chapter.

(3) *Conditions of use*. (i) The drug is intended for use in the treatment of disease due to oxytetracycline-susceptible organisms in beef cattle and nonlactating dairy cattle. It is indicated in the treatment of pneumonia and shipping fever complex associated with *Pasteurella spp.*, *Hemophilus spp.*, *Klebsiella spp.*, foot-rot and diphtheria caused by *Spherophorus necrophorus*, bacterial enteritis (scours) caused by *Escherichia coli*, wooden tongue caused by *Actinobacillus lignieresii*, acute metritis, and wound infections caused by staphylococcal and streptococcal organisms.

(ii) It is administered to cattle at a dosage level of 3 to 5 milligrams per pound of body weight per day. It may be administered intramuscularly or intravenously from a 50 milligram per milliliter solution. It is administered intravenously from a 100 milligram per milliliter solution. Severe foot-rot and the severe forms of the indicated diseases should be treated with 5 milligrams per pound of body weight. Treatment should be continued 24 to

48 hours following remission of disease symptoms, however, not to exceed a total of 4 consecutive days. If no improvement is noted within 24 hours, consult a veterinarian. When injecting the drug intramuscularly, do not inject more than 10 milliliters per site in adult cattle. Reduce the amount injected at each site according to the size of the animal. For very small calves do not use more than 2 milliliters per injection site.

(iii) Not for use in lactating dairy cattle. Discontinue treatment at least 19 days prior to slaughter. When administered intramuscularly within 30 days of slaughter, muscle discoloration may necessitate trimming of the injection site and surrounding tissues.

(d)(1) *Specifications*. The drug contains 50 milligrams of oxytetracycline hydrochloride in each milliliter of sterile solution.

(2) *Sponsor*. See No. 000069 in § 510.600(c) of this chapter.

(3) *Conditions of use*. (i) In beef cattle and nonlactating dairy cattle as follows:

(a) It is used for the treatment of pneumonia and shipping fever complex associated with *Pasteurella spp.* and *Hemophilus spp.*; foot-rot and diphtheria caused by *Spherophorus necrophorus*; bacterial enteritis (scours) caused by *Escherichia coli*; wooden tongue caused by *Actinobacillus lignieresii*; leptospirosis caused by *Leptospira pomona*; wound infections and acute metritis caused by staphylococcal and streptococcal organisms.

(b) Administer by intravenous or intramuscular injection at 3 to 5 milligrams of oxytetracycline per pound of body weight per day. In the treatment of severe foot-rot and severe forms of the indicated diseases, a dosage level of 5 milligrams per pound of body weight per day is recommended.

(c) If the labeling of the drug bears the statement "Federal law restricts this drug to use by or on the order of a licensed veterinarian," it may include additional directions for use in beef cattle and nonlactating dairy cattle for the treatment of anaplasmosis caused by *Anaplasma marginale*, and anthrax caused by *Bacillus anthracis* in which case the drug is given at 3 to 5 milligrams of oxytetracycline per pound of

body weight per day for anthrax, and at 5 milligrams per pound of body weight per day for anaplasmosis.

(ii) In swine as follows:

(a) It is used for the treatment of bacterial enteritis (scours, colibacillosis) caused by *Escherichia coli*; pneumonia caused by *Pasteurella multocida*; and leptospirosis caused by *Leptospira pomona*. Administered to sows as an aid in the control of infectious enteritis (baby pig scours, colibacillosis) in suckling pigs caused by *Escherichia coli*.

(b) Administer by intramuscular injection at 3 to 5 milligrams of oxytetracycline per pound of body weight per day to swine. Administered to sows at 3 milligrams of oxytetracycline per pound of body weight approximately 8 hours before farrowing or immediately after farrowing.

(iii) In poultry (broilers, turkeys, and breeding chickens) as follows:

(a) It is used for the treatment of airsacculitis (air-sac disease, chronic respiratory disease) caused by *Mycoplasma gallisepticum* and *Escherichia coli*; fowl cholera caused by *Pasteurella multocida*; infectious sinusitis caused by *Mycoplasma gallisepticum*; and infectious synovitis caused by *Mycoplasma synoviae*.

(b) Administered subcutaneously to chickens 1 day to 2 weeks of age at 6.25 milligrams of oxytetracycline per bird per day diluted with 1 part of the drug to 3 parts of sterile water; to chickens 2 to 4 weeks of age using the same diluted product at 12.5 milligrams of oxytetracycline per bird; to chickens 4 to 8 weeks of age without dilution at 25 milligrams of oxytetracycline per bird; to chickens 8 weeks of age (broilers and light pullets) at 50 milligrams of oxytetracycline per bird; to adult chickens at 100 milligrams of oxytetracycline per bird.

(c) Administered subcutaneously to turkeys 1 day to 2 weeks of age and 2 to 4 weeks of age at the same dosage as chickens; to turkeys 4 to 6 weeks of age at 50 milligrams of oxytetracycline as the undiluted product per bird; to turkeys 6 to 9 weeks of age at 100 milligrams of oxytetracycline per bird; to turkeys 9 to 12 weeks of age at 150 milligrams of oxytetracycline per bird; to turkeys 12 weeks of age and older at

200 milligrams of oxytetracycline per bird. In light turkey breeds, no more than 25 milligrams per pound of body weight is administered. For the treatment of infectious sinusitis in turkeys, $\frac{1}{4}$ to $\frac{1}{2}$ milliliter of the drug is injected directly into each swollen sinus depending upon the age of the bird and the severity of the condition. At the time that the sinuses are treated, the drug should also be administered subcutaneously to the birds according to the dosage schedule given in paragraph (d)(3)(iii)(c) of this section. If refilling of the sinuses occurs, the treatment may be repeated in 5 to 7 days.

(iv) Treatment of all diseases should be instituted early. Treatment should continue for 24 to 48 hours beyond the remission of disease symptoms, but not exceed a total of 4 consecutive days. If no improvement is noted within 24 to 48 hours, diagnosis and therapy should be reevaluated.

(v) When injecting intramuscularly in adult livestock, do not inject more than 10 milliliters at any one site. The volume administered per injection site should be reduced according to age and body size so that 1 or 2 milliliters are injected in smaller animals such as small calves and young pigs. Intravenous administration is recommended in cattle when daily dosage exceeds 50 milliliters.

(vi) Treatment must be discontinued at least 5 days prior to slaughter for chickens and turkeys and at least 22 days prior to slaughter for cattle and swine. When administered intramuscularly to animals within 30 days of slaughter, muscle discoloration may necessitate trimming of the injection site(s) and surrounding tissues during the dressing procedure.

(vii) Not for use in lactating dairy animals. Do not administer to laying hens unless the eggs are used for hatching only.

(e)(1) *Specifications.* Each milliliter of sterile solution contains 100 milligrams of oxytetracycline.

(2) *Sponsor.* See No. 000069 in § 510.600(c) of this chapter.

(3) *Conditions of use—(i) Beef cattle and nonlactating dairy cattle—(a) Amount.* 3 to 5 milligrams of oxytetracycline per pound of body weight per

day; 5 milligrams per pound of body weight per day for treatment of anaplasmosis, severe foot-rot, and severe cases of other indicated diseases.

(b) *Indications for use.* Treatment of diseases due to oxytetracycline-susceptible organisms as follows: Pneumonia and shipping fever complex associated with *Pasteurella* spp. and *Hemophilus* spp., foot-rot and diphtheria caused by *Fusobacterium necrophorum*, bacterial enteritis (scours) caused by *Escherichia coli*, wooden tongue caused by *Actinobacillus lignieresii*, leptospirosis caused by *Leptospira pomona*, and wound infections and acute metritis caused by *Staphylococcus* spp. and *Streptococcus* spp. If labeled for use by or on the order of a licensed veterinarian, it may be used for the treatment of anaplasmosis caused by *Anaplasma marginale* and anthrax caused by *Bacillus anthracis*.

(c) *Limitations.* Administer intramuscularly. Treatment of all diseases should be instituted early and continue for 24 to 48 hours beyond remission of disease symptoms, but not to exceed a total of 4 consecutive days. Consult your veterinarian if no improvement is noted within 48 hours. Do not inject more than 10 milliliters per site in adult cattle, reducing the volume according to age and body size to 1 to 2 milliliters in small calves. Exceeding the highest recommended dose of 5 milligrams per pound of body weight, administering at recommended levels for more than 4 consecutive days, and/or exceeding 10 milliliters intramuscularly per injection site may result in antibiotic residues beyond the withdrawal time. Discontinue treatment at least 15 days prior to slaughter. Not for use in lactating dairy cattle.

(ii) *Swine*—(a) *Amount.* 3 to 5 milligrams of oxytetracycline per pound of body weight per day. Sows: 3 milligrams of oxytetracycline per pound of body weight, administered once, approximately 8 hours before farrowing or immediately after completion of farrowing.

(b) *Indications for use.* For treatment of bacterial enteritis (scours, colibacillosis) caused by *Escherichia coli*, pneumonia caused by *Pasteurella multocida*, and leptospirosis caused by *Leptospira pomona*. Sows: as an aid in

control of infections enteritis (baby pig scours, colibacillosis) in suckling pigs caused by *Escherichia coli*.

(c) *Limitations.* Administer intramuscularly. Do not inject more than 5 milliliters per site in adult swine, reducing the volume according to age and body size to 1 to 2 milliliters in young pigs. Discontinue treatment at least 22 days prior to slaughter.

(f)(1) *Specifications.* The drug contains 50 milligrams of oxytetracycline hydrochloride in each milliliter of sterile solution.

(2) *Sponsor.* See No. 010271 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) Use in beef cattle, beef calves, nonlactating dairy cattle, and dairy calves for the treatment of pneumonia and shipping fever complex associated with *Pasteurella* spp. and *Hemophilus* spp.; foot-rot and diphtheria caused by *Sphaerophorus necrophorus*; bacterial enteritis (scours) caused by *Escherichia coli*; wooden tongue caused by *Actinobacillus lignieresii*; leptospirosis caused by *Leptospira pomona*; wound infections, acute metritis, and traumatic injury caused by staphylococcal and streptococcal organisms.

(ii) Administer by intramuscular injection at 3 to 5 milligrams of oxytetracycline per pound of body weight per day. In the treatment of leptospirosis, severe foot-rot, and severe forms of the indicated diseases, administer 5 milligrams per pound of body weight per day.

(iii) Treatment should continue for 24 to 48 hours beyond remission of disease symptoms, but not to exceed a total of 4 consecutive days. Treat at the first clinical signs of disease. If no improvement is noted within 48 hours, consult a veterinarian for diagnosis and therapy.

(iv) In adult livestock, do not inject more than 10 milliliters at any one site. Reduce the volume administered per injection site according to age and body size. In calves weighing 100 pounds or less inject only 2 milliliters per site.

(v) Discontinue treatment at least 22 days prior to slaughter. Exceeding the recommended dosage level or duration of treatment may result in antibiotic residues beyond the withdrawal time.

(vi) Not for use in lactating dairy animals.

(g)(1) *Specifications.* Each milliliter of sterile solution contains 100 milligrams of oxytetracycline as oxytetracycline hydrochloride.

(2) *Sponsor.* See No. 054273 in § 510.600(c) of this chapter.

(3) *Conditions of use.* The drug is used for the treatment of diseases due to oxytetracycline-susceptible organisms as follows:

(i) *Beef cattle, beef calves, nonlactating dairy cattle, and dairy calves—(a) Amount.* 3 to 5 milligrams of oxytetracycline per pound of body weight per day.

(b) *Indications for use.* For the treatment of pneumonia and shipping fever complex associated with *Pasteurella spp.*, *Hemophilus spp.*, or *Klebsiella spp.*

(c) *Limitations.* Administer by intramuscular or intravenous injection. In severe forms of the indicated diseases, administer 5 milligrams of oxytetracycline per pound of body weight per day. Continue treatment 24 to 48 hours following remission of disease symptoms, not to exceed a total of 4 consecutive days. If no improvement is noted within 48 hours, consult a veterinarian. Do not inject more than 10 milliliters per injection site intramuscularly in adult cattle; no more than 1 milliliter per site in calves weighing 100 pounds or less. Discontinue treatment at least 20 days prior to slaughter.

(ii) *Swine—(a) Amount.* 3 to 5 milligrams of oxytetracycline per pound of body weight per day. Sows: Administer once 3 milligrams of oxytetracycline per pound of body weight, approximately 8 hours before farrowing or immediately after completion of farrowing.

(b) *Indications for use.* For treatment of bacterial enteritis (scours, colibacillosis) caused by *Escherichia coli*, pneumonia caused by *Pasteurella multocida*, and leptospirosis caused by *Leptospira pomona*. Sows: As an aid in control of infectious enteritis (baby pig scours, colibacillosis) in suckling pigs caused by *Escherichia coli*.

(c) *Limitations.* Administer intramuscularly. If no improvement is noted within 24 hours, consult a veter-

inarian. Do not inject more than 5 milliliters per site. Discontinue treatment at least 20 days prior to slaughter.

(h)(1) *Specifications.* Each milliliter of sterile solution contains 50 or 100 milligrams of oxytetracycline hydrochloride.

(2) *Sponsor.* See No. 054273 in § 510.600(c) of this chapter.

(3) *Conditions of use—(i) Amount.* The drug is used in beef cattle, beef calves, nonlactating dairy cattle, and dairy calves as follows: 3 to 5 milligrams of oxytetracycline hydrochloride per pound of body weight per day; 5 milligrams per pound of body weight per day for treatment of severe forms of the indicated diseases.

(ii) *Indications for use.* The drug is used for treatment of bacterial pneumonia and shipping fever complex associated with *Pasteurella spp.*; foot-rot and calf diphtheria caused by *Sphaerophorus necrophorus*; bacterial enteritis (scours) caused by *Escherichia coli*; wooden tongue caused by *Actinobacillus lignieresii*; wound infections, acute metritis, and traumatic injury caused by staphylococcal and streptococcal organisms.

(iii) *Limitations.* Administer 50-milligram-per-milliliter solution intramuscularly; administer 100-milligram-per-milliliter solution intravenously. Continue treatment 24 to 48 hours following remission of disease symptoms, not to exceed a total of 4 consecutive days. If no improvement is noted within 24 to 48 hours, consult a veterinarian for diagnosis and therapy. When injecting the drug intramuscularly, do not inject more than 10 milliliters per site in adult cattle. Reduce the volume administered per injection site according to age and body size. In calves weighing 100 pounds or less, do not inject more than 2 milliliters intramuscularly per site. Discontinue treatment at least 22 days before slaughter. Not for use in lactating dairy animals.

(i)(1) *Specifications.* Each milliliter of sterile solution contains 50 milligrams of oxytetracycline hydrochloride.

(2) *Sponsor.* See No. 053617 in § 510.600(c) of this chapter.

(3) *Conditions of use—(i) Amount.* The drug is used in beef cattle, beef calves, nonlactating dairy cattle, and

dairy calves as follows: Administer 3 to 5 milligrams of the oxytetracycline hydrochloride intramuscularly per pound of body weight per day.

(ii) *Indications for use.* The drug is used for treatment of bacterial pneumonia and shipping fever complex associated with *Pasteurella* spp.; foot rot and diphtheria caused by *Spherothorus necrophorus*; bacterial enteritis (scours) caused by *Escherichia coli*; wooden tongue caused by *Actinobacillus lignieresii*; wound infections and acute metritis caused by staphylococcal and streptococcal organisms susceptible to oxytetracycline.

(iii) *Limitations.* In severe forms of the indicated diseases, administer the equivalent of 5 milligrams of oxytetracycline hydrochloride per pound of body weight per day. Continue treatment 24 to 48 hours following remission of disease symptoms, not to exceed a total of 4 consecutive days. If no improvement is noted within 24 to 48 hours, consult a veterinarian for diagnosis and therapy. In adult livestock, do not inject more than 10 milliliters at any one site. Reduce the volume administered per injection site according to age and body size. In calves weighing 100 pounds or less inject only 2 milliliters per site. Discontinue treatment at least 18 days before slaughter. Not for use in lactating dairy cattle.

(j)(1) *Specifications.* Each milliliter of sterile solution contains 100 milligrams of oxytetracycline hydrochloride.

(2) *Sponsor.* See No. 010271 in § 510.600(c) of this chapter.

(3) *Related tolerances.* See § 556.500 of this chapter.

(4) *Special considerations.* Labeling shall bear the following statements: Treatment should be continued 24 to 48 hours following remission of disease symptoms but not to exceed a total of 4 consecutive days. If no improvement noted within 24 to 48 hours, consult a veterinarian.

(5) *Conditions of use in beef cattle and nonlactating dairy cattle—(i) Amount.* Three to 5 milligrams per pound of body weight per day. In severe cases, 5 milligrams per pound of body weight.

(ii) *Indications for use.* Treatment of pneumonia and shipping fever complex associated with *Pasteurella* spp. and *Hemophilus* spp. sensitive to oxytetracycline.

(iii) *Limitations.* Administer intravenously only. Not for use in lactating dairy cattle. Discontinue treatment at least 19 days before slaughter.

(k)(1) *Specifications.* Each milliliter of sterile solution contains either 50 or 100 milligrams of oxytetracycline hydrochloride.

(2) *Sponsor.* See No. 000864 in § 510.600(c) of this chapter.

(3) *Conditions of use in beef cattle and nonlactating dairy cattle.*

(i) *Amount.* 3 to 5 milligrams per pound of body weight daily, 5 milligrams per pound for anaplasmosis, severe foot rot, and severe forms of other diseases.

(ii) *Indications for use.* Treatment of diseases due to oxytetracycline-susceptible organisms as follows: pneumonia and shipping fever complex associated with *Pasteurella* spp. and *Hemophilus* spp.; foot rot and diphtheria caused by *Fusobacterium necrophorum*; bacterial enteritis (scours) caused by *Escherichia coli*; wooden tongue caused by *Actinobacillus lignieresii*; leptospirosis caused by *Leptospira pomona*; acute metritis and wound infections caused by staphylococcal and streptococcal organisms; if labeled for use by or on the order of a licensed veterinarian, it may be used for treatment of anaplasmosis caused by *Anaplasma marginale* and anthrax caused by *Bacillus anthracis*.

(iii) *Limitations.* Administer by intravenous injection. Treatment should be continued 24 to 48 hours following remission of disease symptoms, but not to exceed a total of 4 consecutive days. If no improvement occurs within 24 to 48 hours, reevaluate diagnosis and therapy. Discontinue use at least 19 days prior to slaughter. Not for use in lactating dairy cattle.

[40 FR 13858, Mar. 27, 1975]

EDITORIAL NOTE: For FEDERAL REGISTER citations affecting § 522.1662a, see the List of CFR Sections Affected in the Finding Aids section of this volume.

§ 522.1662b

§ 522.1662b Oxytetracycline hydrochloride with lidocaine injection.

(a) *Specifications.* The drug contains 50 or 100 milligrams of oxytetracycline hydrochloride and 2 percent lidocaine in each milliliter of sterile aqueous solution.

(b) *Sponsor.* See No. 000069 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is indicated for use in the treatment of diseases of dogs caused by pathogens sensitive to oxytetracycline hydrochloride including treatment for the following conditions in dogs caused by susceptible microorganisms: Bacterial infections of the urinary tract caused by *Hemolytic staphylococcus*, *Streptococcus spp.*, Bacterial pulmonary infections caused by *Brucella bronchiseptica*, *Streptococcus pyogenes*, *Staphylococcus aureus*, secondary bacterial infections caused by *Micrococcus pyogenes var. albus*, *Brucella bronchiseptica*, *Streptococcus spp.*

(2) The drug is administered intramuscularly at a recommended daily dosage to dogs at 5 milligrams per pound of body weight administered in divided doses at 6 to 12 hour intervals. Therapy should be continued for at least 24 hours after all symptoms have subsided.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13858, Mar. 27, 1975, as amended at 48 FR 30615, July 5, 1983]

§ 522.1680 Oxytocin injection.

(a) *Specifications.* Each milliliter of oxytocin injection contains 20 U.S.P. units of oxytocin.

(b) *Sponsors.* See Nos. 000010, 000402, 000693, 000856, 000857, 000864, 010271, 032420, 053617, and 054273 in § 510.600(c) of this chapter.

(c) *Conditions of use.*—(1) *Amount.*—(i) *Obstetrical.* Administer drug intra-

¹ These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bio-equivalency and safety information.

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venously, intramuscularly, or subcutaneously under aseptic conditions as indicated. The following dosages are recommended and may be repeated as conditions require:

	ml	U.S.P. units
Cats	0.25 to 0.5	5 to 10.
Dogs	0.25 to 1.5	5 to 30.
Pigs, Sows	1.5 to 2.5	30 to 50.
Cows, Horses	5.0	100.

(ii) *Milk letdown.* Intravenous administration is desirable. The following dosage is recommended and may be repeated as conditions require:

	ml	U.S.P. units
Cows	0.5 to 1.0	10 to 20.
Sows	0.25 to 1.0	5 to 20.

(2) *Indications for use.* Oxytocin may be used as a uterine contractor to precipitate and accelerate normal parturition and postpartum evacuation of uterine debris. In surgery it may be used postoperatively following cesarean section to facilitate involution and resistance to the large inflow of blood. It will contract smooth muscle cells of the mammary gland for milk letdown if the udder is in proper physiological state.

(3) *Limitations.* Do not use in dystocia due to abnormal presentation of fetus until correction is accomplished. For prepartum usage, full relaxation of the cervix should be accomplished either naturally or by administration of estrogen prior to oxytocin therapy. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(Sec. 512(e), 82 Stat. 345-347 (21 U.S.C. 360b(e)))

[44 FR 63097, Nov. 2, 1979; 45 FR 1019, Jan. 4, 1980, as amended at 52 FR 18691, May 19, 1987; 52 FR 25212, July 6, 1987; 53 FR 36023, Sept. 25, 1987; 53 FR 32610, Aug. 26, 1988; 53 FR 40728, Oct. 18, 1988]

§ 522.1698 Pentazocine lactate injection.

(a) *Specifications.* Each milliliter of sterile aqueous solution contains pentazocine lactate equivalent to 30 milligrams of pentazocine base.

(b) *Sponsor.* See No. 000934 in § 510.600(c) of this chapter.

(c) *Conditions of use.*—(1) *Horses.*—(i) *Amount.* 0.15 milligram of pentazocine base per pound of body weight per day.

(ii) *Indications for use.* For symptomatic relief of pain due to colic.

(iii) *Limitations.* Administer intravenously or intramuscularly. Intravenous injections are given slowly in the jugular vein. In cases of severe pain, a second dose is recommended intramuscularly 10 to 15 minutes after the initial dose at the same level. Not for use in horses intended for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(2) *Dogs.*—(i) *Amount.* 0.75 to 1.50 milligrams of pentazocine base per pound of body weight.

(ii) *Indications for use.* For amelioration of pain accompanying postoperative recovery, fracture, trauma, and spinal disorders.

(iii) *Limitations.* Administer intramuscularly only. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[42 FR 31450, June 21, 1977, as amended at 42 FR 36995, July 19, 1977; 47 FR 5409, Feb. 5, 1982]

§ 522.1704 Sodium pentobarbital injection.

(a)(1) *Specifications.* Sodium pentobarbital injection is sterile and contains in each milliliter 64.8 milligrams of sodium pentobarbital.

(2) *Sponsor.* See No. 011716 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) The drug is indicated for use as a general anesthetic in dogs and cats. Although it may be used as a general surgical anesthetic for horses, it is usually given at a lower dose to cause sedation and hypnosis and may be supplemented with a local anesthetic. It may also be used in dogs for the symptomatic treatment of strychnine poisoning.

(ii) The drug is administered intravenously "to effect". For general surgical anesthesia, the usual dose is 11 to 13 milligrams per pound of body weight. For sedation, the usual dose is approximately 2 milligrams per pound of body weight. For relieving convulsive seizures in dogs, when caused by strychnine, the injection should be ad-

ministered intravenously "to effect". The drug may be given intraperitoneally if desired. However, the results of such injections are less uniform. When given intraperitoneally, it is administered at the same dosage level as for intravenous administration. The dose must be reduced for animals showing under-nourishment, toxemia, shock and similar conditions.

(iii) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(b)(1) *Specifications.* Sodium pentobarbital injection is sterile and contains in each milliliter 65 milligrams of sodium pentobarbital.

(2) *Sponsor.* See 000402 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) The drug is indicated for use as a general anesthetic in dogs and cats.

(ii) The drug is administered intravenously "to effect." For general anesthesia, the usual dose is 13 milligrams per pound of body weight.

(iii) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13858, Mar. 27, 1975, as amended at 45 FR 83453, Dec. 19, 1980; 52 FR 25212, July 6, 1987]

§ 522.1720 Phenylbutazone injection.

(a) *Specifications.* The drug contains 100 or 200 milligrams of phenylbutazone in each milliliter of sterile aqueous solution.

(b) *Sponsors.* (1) Approval for use of the 200 milligrams per milliliter drug in dogs and horses: See sponsor Nos. 000031, 017220, 053617, and 010719 in § 510.600(c) of this chapter.

(2) Approval for use of the 200 milligrams per milliliter drug in horses: See sponsor Nos. 010271, 000010, 000364, 000693, and 000402 in § 510.600(c) of this chapter.

(3) Approval for use of the 100 milligrams per milliliter drug in dogs and horses: See sponsor No. 000856 in § 510.600(c) of this chapter.

(4) Approval for use of the 200 milligrams per milliliter drug in dogs: See sponsor No. 000864 in § 510.600(c) of this chapter.

(c) *Conditions of use for dogs.* (1) It is used for the relief of inflammatory

conditions associated with the musculoskeletal system.¹

(2) It is administered intravenously at a dosage level of 10 milligrams per pound of body weight daily in 3 divided doses, not to exceed 800 milligrams daily regardless of weight. Limit intravenous administration to 2 successive days. Oral medication may follow.¹

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

(d) *Conditions of use for horses.* (1) It is used for the relief of inflammatory conditions associated with the musculoskeletal system.¹

(2) It is administered intravenously at a dosage level of 1 to 2 grams per 1,000 pounds of body weight daily in 3 divided doses, not to exceed 4 grams daily. Limit intravenous administration to not more than 5 successive days.¹

(3) Not for use in animals intended for food.¹

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

[40 FR 13858, Mar. 27, 1975, as amended at 40 FR 18994, May 1, 1975; 40 FR 23847, June 3, 1975; 41 FR 9150, Mar. 3, 1976; 41 FR 55175, Dec. 17, 1976; 46 FR 48642, Oct. 2, 1981; 47 FR 30668, July 13, 1982; 50 FR 49373, Dec. 2, 1985; 52 FR 25212, July 6, 1987; 52 FR 36023, Sept. 25, 1987]

§ 522.1800 Piperacetazine injection.

(a) *Specifications.* The drug is a sterile aqueous solution and each milliliter contains piperacetazine hydrochloride equivalent to 2 milligrams of piperacetazine.

(b) *Sponsor.* See No. 011716 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is intended for use in dogs and cats as a tranquilizer, sedative, and antiemetic agent and for the symptomatic relief of pruritis.

(2) It is administered intramuscularly, intravenously, or subcutaneously; method of administration depends upon the effect desired. It is adminis-

¹ These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

tered at a recommended average dose that ranges from 0.5 to 2 milligrams per 10 pounds of body weight, depending on the effect desired and the response of the patient. Subsequent doses are adjusted as indicated. Treatment is repeated as necessary. Parenteral treatment may be followed by administration of the drug in tablet form, as indicated.

(3) It is not to be used in conjunction with organophosphates and/or procaine hydrochloride because phenothiazines may potentiate the toxicity of organophosphates and the activity of procaine hydrochloride.

(4) For use only by or on the order of a licensed veterinarian.

§ 522.1820 Pituitary luteinizing hormone for injection.

(a) *Specifications.* The drug is a lyophilized pituitary extract. Each 6-milliliter vial contains an amount equivalent to 25 milligrams of standard pituitary luteinizing hormone and is reconstituted for use by addition of 5 milliliters of 0.9 percent aqueous sodium chloride solution.

(b) *Sponsor.* No. 000061 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is an aid in the treatment of breeding disorders related to pituitary hypofunction in cattle, horses, swine, sheep, and dogs.

(2) Preferably given by intravenous injection, it may be administered subcutaneously; dosage is as follows: Cattle and horses, 25 mg; swine, 5 mg; sheep, 2.5 mg, and dogs, 1.0 mg. Treatment may be repeated in 1 to 4 weeks, or as indicated.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13858, Mar. 27, 1975, as amended at 52 FR 7832, Mar. 13, 1987]

§ 522.1822 Follicle stimulating hormone-pituitary for injection.

(a) *Specifications.* The drug is a lyophilized pituitary extract material. Each 10-milliliter vial contains an amount equivalent to 50 milligrams of standard porcine follicle stimulating hormone and is reconstituted for use

by addition of 10 milliliters of 0.9 percent aqueous sodium chloride solution.

(b) *Sponsor.* No. 000061 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used as a supplemental source of follicle stimulating hormone where there is a general deficiency in cattle, horses, sheep, swine, and dogs.

(2) It is administered intramuscularly, subcutaneously, or intravenously as follows:

Animal	Dosage in milligrams
Cattle and horses	10-50
Sheep and swine	5-25
Dogs	5-15

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[41 FR 27033, July 1, 1976, as amended at 52 FR 7832, Mar. 13, 1987]

§ 522.1850 Polysulfated glycosaminoglycan.

(a) *Specifications.* Each 1-milliliter ampule of sterile aqueous solution contains 250 milligrams of polysulfated glycosaminoglycan.

(b) *Sponsor.* See No. 010797 in § 510.600(c) of this chapter.

(c) *Conditions of use.*—(1) *Indications for use.* It is used in horses. Polysulfated glycosaminoglycan is recommended for the treatment of noninfectious degenerative and/or traumatic joint dysfunction and associated lameness of the carpal joint.

(2) *Amount.* 250 milligrams once a week for 5 weeks.

(3) *Limitations.* For intra-articular use. The joint area must be shaved, cleaned, and sterilized as in a surgical procedure prior to injection. If the joint reacts with excessive inflammation, after intra-articular treatment, cease therapy. Not for use in horses intended for food. Do not use in horses intended for breeding. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[49 FR 47830, Dec. 7, 1984]

§ 522.1862 Sterile pralidoxime chloride.

(a) *Chemical name.* 2-Formyl-1-methylpyridinium chloride oxime.

(b) *Specifications.* Sterile pralidoxime chloride is packaged in vials. Each vial contains 1 gram of sterile pralidoxime chloride powder and includes directions for mixing this gram with 20 cubic centimeters of sterile water for injection prior to use.

(c) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(d) *Conditions of use.* (1) It is used in horses, dogs, and cats as an antidote in the treatment of poisoning due to those pesticides and chemicals of the organophosphate class which have anticholinesterase activity in horses, dogs, and cats.

(2) It is administered as soon as possible after exposure to the poison. Before administration of the sterile pralidoxime chloride, atropine is administered intravenously at a dosage rate of 0.05 milligram per pound of body weight, followed by administration of an additional 0.15 milligram of atropine per pound of body weight administered intramuscularly. Then the appropriate dosage of sterile pralidoxime chloride is administered slowly intravenously. The dosage rate for sterile pralidoxime chloride when administered to horses is 2 grams per horse. When administered to dogs and cats, it is 25 milligrams per pound of body weight. For small dogs and cats, sterile pralidoxime chloride may be administered either intraperitoneally or intramuscularly. A mild degree of atropinization should be maintained for at least 48 hours. Following severe poisoning, a second dose of sterile pralidoxime chloride may be given after 1 hour if muscle weakness has not been relieved.

(3) For use only by or on the order of a licensed veterinarian.

[40 FR 13858, Mar. 27, 1975, as amended at 49 FR 32061, Aug. 10, 1984]

§ 522.1870 Praziquantel injectable solution.

(a) *Specification.* Each milliliter contains 56.8 milligrams of praziquantel.

(b) *Sponsor.* See 000859 in § 510.600(c) of this chapter.

(c) *Conditions of use.*—(1) *Dogs.*—(i) *Amount.* For dogs 5 pounds and under, 0.3 milliliter (17.0 milligrams); for 6 to 10 pounds, 0.5 milliliter (28.4 milli-

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grams); for 11 to 25 pounds, 1.0 milliliter (56.8 milligrams); if over 25 Pounds, 0.2 milliliter (11.4 milligrams) per 5 pounds body weight to a maximum of 3 milliliters (170.4 milligrams).

(ii) *Indications for use.* For removal of canine cestodes *Dipylidium caninum*, *Taenia pisiformis*, and *Echinococcus granulosus*.

(iii) *Limitations.* For subcutaneous or intramuscular use; not intended for use in puppies less than 4 weeks of age; Federal law restricts the drug to use by or on the order of a licensed veterinarian.

(2) *Cats*—(i) *Amount.* For cats under 5 pounds, 0.2 milliliter (11.4 milligrams); 5 to 10 pounds, 0.4 milliliter (22.7 milligrams); 11 pounds and over, 0.6 milliliter (34.1 milligrams) maximum.

(ii) *Indications for use.* For removal of feline cestodes *Dipylidium caninum* and *Taenia taeniaeformis*.

(iii) *Limitations.* For subcutaneous or intramuscular injection only. Not intended for use in kittens less than 6 weeks of age. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[46 FR 10464, Feb. 3, 1981, as amended at 47 FR 6617, Feb. 16, 1982]

§ 522.1880 Sterile prednisolone suspension.

(a) *Specifications.* Each milliliter of sterile aqueous suspension contains 10 or 25 milligrams of prednisolone.

(b) *Sponsor.* See No. 010719 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is indicated in the treatment of dogs, cats, and horses for use as an anti-inflammatory agent.¹

(2) The drug is administered as follows and treatment may be repeated when necessary:¹

¹These conditions are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

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Species	Intramuscular	Intra-articular
Horse	50-200 milligrams	40-80 milligrams
Dog	10-30 milligrams	10-20 milligrams
Cat	5-10 milligrams	10-20 milligrams

(3) Corticosteroids administered orally or parenterally to animals may induce the first stage of parturition when administered during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis.

(4) Not for use in horses intended for food.¹

(5) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

§ 522.1881 Sterile prednisolone acetate aqueous suspension.

(a) *Specifications.* Each milliliter of sterile aqueous suspension contains 25 milligrams of prednisolone acetate.

(b) *Sponsor.* See No. 000061 in § 510.600(c) of this chapter.

(c) *NAS/NRC status.* The conditions of use are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified in § 514.111 of this chapter but may require bioequivalency and safety information.

(d) *Conditions of use.* (1) The drug is indicated in the treatment of dogs, cats, and horses for conditions requiring an anti-inflammatory agent. The drug is indicated for the treatment of acute musculoskeletal inflammations such as bursitis, carpalitis, and spondylitis. The drug is indicated as supportive therapy in nonspecific dermatosis such as summer eczema and atopy. The drug may be used as supportive therapy pre- and post-operatively and for various stress conditions when corticosteroids are required while the animal is being treated for a specific condition.

(2) The drug is administered to horses intra-articularly at a dosage level of 50 to 100 milligrams. The dose may be repeated when necessary. If no response is noted after 3 or 4 days, the possibility must be considered that the condition is unresponsive to prednisolone therapy. The drug is admini-

tered to dogs and cats intramuscularly at a dosage level of 10 to 50 milligrams. The dosage may be repeated when necessary. If the condition is of a chronic nature, an oral corticosteroid may be given as a maintenance dosage. The drug may be given intrarticularly to dogs and cats at a dosage level of 5 to 25 milligrams. The dose may be repeated when necessary after 7 days for two or three doses.

(3) The labeling shall comply with the requirements of § 510.410 of this chapter for corticosteroids.

(4) Not for use in horses intended for food.

(5) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[52 FR 23032, June 17, 1987]

§ 522.1883 Prednisolone sodium phosphate injection, sterile.

(a)(1) *Specifications.* Each milliliter contains 20 milligrams of prednisolone sodium phosphate (equivalent to 14.88 milligrams of prednisolone) in sterile aqueous solution.

(2) *Sponsor.* See No. 000864 in § 510.600(c) of this chapter.

(3) *Conditions of use.*—(i) It is used in treatment of dogs when a rapid adrenal glucocorticoid and/or anti-inflammatory effect is necessary.¹

(ii) It is administered intravenously in a dosage of 2½ to 5 milligrams of prednisolone sodium phosphate per pound of body weight, initially for shock and shock-like states, followed by equal maintenance doses at 1-, 3-, 6-, or 10-hour intervals as determined by the condition of the animal. If permanent use is required, oral therapy (tablets) may be substituted. If therapy is to be withdrawn after prolonged use, reduce daily dose gradually over a number of days.

(iii) Do not use in viral infections. Except in emergency therapy, do not use with tuberculosis, chronic nephritis, Cushing's disease, or peptic ulcers. With infections, use appropriate antibacterial therapy with, and for at least 3 days after, discontinuance of use and disappearance of all signs of infection.¹

(iv) Clinical and experimental data have demonstrated that corticosteroids administered orally or parenterally to animals may induce the first

stage of parturition when administered during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis.

(v) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

(b) [Reserved]

[43 FR 29769, July 11, 1978, as amended at 49 FR 23834, June 8, 1984]

§ 522.1884 Prednisolone sodium succinate injection.

(a) *Chemical name.* 11 beta, 17, 21-Trihydroxypregna-1, 4-diene-3, 20-dione 21-succinate sodium salt.

(b) *Specifications.* Each milliliter of prednisolone sodium succinate injection contains: Prednisolone sodium succinate equivalent in activity to 10, 20, or 50 milligrams of prednisolone.

(c) *Sponsor.* See No. 000009 in § 510.600(c) of this chapter for products containing 10, 20, and 50 milligrams equivalent prednisolone activity per milliliter for use in horses, dogs, and cats as provided in paragraphs (d)(1), (2) (i), (ii), and (iii) of this section. See No. 000402 in § 510.600(c) of this chapter for a product containing 10 milligrams equivalent prednisolone activity per milliliter for use in horses as provided in paragraph (d)(2)(iv) of this section.

(d) *Conditions of use.* (1) The drug is intended for the treatment of horses, dogs, and cats.¹

(2)(i) The dosage for horses is 50 to 100 milligrams as an initial dose given intravenously over a period of one-half to 1 minute, or intramuscularly, and may be repeated in inflammatory, allergic, or other stress conditions at intervals of 12, 24, or 48 hours, depending upon the size of the animal, the severity of the condition and the response to treatment.¹

(ii) In dogs, the drug is administered intravenously at a range of 2.5 to 5 milligrams per pound of body weight

¹These conditions are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

as an initial dose followed by maintenance doses at 1, 3, 6, or 10 hour intervals, as determined by the condition of the animal, for treatment of shock.

(iii) In dogs and cats, the drug may be given intramuscularly for treatment of inflammatory, allergic and less severe stress conditions, where immediate effect is not required, at 1 to 5 milligrams ranging upward to 30 to 50 milligrams in large breeds of dogs. Dosage may be repeated in 12 to 24 hours and continued for 3 to 5 days if necessary. If permanent corticosteroid effect is required oral therapy with prednisolone tablets may be substituted.

(iv) In horses, 50 to 100 milligrams as an initial dose given intravenously over a period of ¼ to 1 minute. May be repeated in inflammatory, allergic, or other stress conditions at intervals of 12, 24, or 48 hours, depending upon the size of the animal, the severity of the condition and the response to treatment. Not for use in horses intended for food. Clinical and experimental data have demonstrated that corticosteroids administered orally or parenterally to animals may induce the first stage of parturition when administered late in pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

[40 FR 13858, Mar. 27, 1975, as amended at 46 FR 13215, Feb. 20, 1981; 46 FR 33513, June 30, 1981; 52 FR 25212, July 6, 1987]

§ 522.1885 Prednisolone tertiary butylacetate suspension.

(a) *Specifications.* Prednisolone tertiary butylacetate (Pregna-1,4-diene-3, 20-dione-11B, 17α 21-triol 21-(3,3, dimethyl butyrate) suspension contains 20 milligrams of prednisolone tertiary butylacetate per milliliter. It is sterile.

(b) *Sponsor.* See No. 000006 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is used as an anti-inflammatory agent in horses, dogs, and cats.¹

(2) It is administered to horses intramuscularly at a dosage level of 100 to 300 milligrams and intrasynovially at a dosage level of 50 to 100 milligrams. It

is administered intramuscularly to dogs and cats at a dosage level of 1 milligram per 5 pounds of body weight and intrasynovially at a dosage level of 10 to 20 milligrams. Intramuscular retreatment of horses in 24 to 48 hours may be necessary, depending on the general condition of the animal and the severity and duration of the disease.¹

(3) Clinical and experimental data have demonstrated that corticosteroids administered orally or parenterally to animals may induce the first stage of parturition when administered late in pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis.¹

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

§ 522.1890 Sterile prednisone suspension.

(a) [Reserved]

(b)(1) *Specifications.* Each milliliter of sterile aqueous suspension contains 10 to 40 milligrams of prednisone.

(2) *Sponsor.* See 000061 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) *Amount.* Administer intramuscularly as follows:

(a) *Horses.* 100 to 400 milligrams, repeating if necessary. If no response is observed after 3 to 4 days of therapy, reevaluate diagnosis.¹

(b) *Dogs and cats.* 0.25 to 1.0 milligram per pound of body weight for 3 to 5 days or until a response is noted. Treatment may be continued with an orally administered dose.¹

(ii) *Indications for use.* It is used for conditions requiring an anti-inflammatory agent.¹

(iii) *Limitations.*¹ Do not use in viral infections. Except in emergency therapy, do not use in animals with tuberculosis, chronic nephritis, or Cushing's disease. With infections, use appropriate antibacterial therapy with and for at least 3 days after discontinuance of use and disappearance of

¹ These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

all signs of infection. Clinical and experimental data have demonstrated that corticosteroids administered orally or parenterally to animals may induce the first stage of parturition when administered during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis. Not for use in horses intended for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(Sec. 512(e), 82 Stat. 345-347 (21 U.S.C. 360b(e)))

[45 FR 13446, Feb. 29, 1980, as amended at 50 FR 6160, Feb. 14, 1985; 52 FR 7832, Mar. 13, 1987]

§ 522.1920 Prochlorperazine, isopropamide for injection.

(a) *Specifications.* Prochlorperazine, isopropamide for injection, veterinary, contains in each milliliter, 6 milligrams of prochlorperazine edisylate (equivalent to 4 milligrams prochlorperazine), and 0.38 milligrams of isopropamide iodide (equivalent to 0.28 milligrams of isopropamide) in buffered aqueous solution.

(b) *Sponsor.* See No. 011519 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used in dogs and cats in which gastrointestinal disturbances are associated with emotional stress.

(2) Dosage is administered by subcutaneous injection twice daily as follows:

Weight of animal in pounds	Dosage in Milliliters
Up to 4	0.25
5 to 14	0.5-1
15 to 30	2-3
30 to 45	3-4
45 to 60	4-5
Over 60	6

Following the last injection, administer prochlorperazine and isopropamide sustained release capsules as indicated.

(3) For use only by or on the order of a licensed veterinarian.

§ 522.1940 Progesterone and estradiol benzoate in combination.

(a) *Chemical names.* (1) Progesterone: 4-Pregnene-3,20-dione.

(2) Estradiol benzoate: 1,3,5(10)-Estratriene-3,17-beta-diol 3-benzoate.

(b) *Sponsor.* See No. 000033 for use as provided for in paragraphs (d) (1) and (2) of this section; see No. 021641 for use as provided for in paragraph (d)(2) of this section.

(c) *Related tolerances.* See §§ 556.240 and 556.540 of this chapter.

(d) *Conditions of use.* It is used for implantation in animals as follows:

(1) *Suckling beef calves*—(i) *Amount.* 100 milligrams of progesterone and 10 milligrams of estradiol benzoate per dose.

(ii) *Indications for use.* Increased rate of weight gain.

(iii) *Limitations.* For use in suckling beef calves (at least 45 days of age) up to 400 pounds of body weight; do not use in bull calves intended for reproduction; for subcutaneous ear implantation, one dose per animal.

(2) *Steers*—(i) *Amount.* 200 milligrams of progesterone and 20 milligrams of estradiol benzoate per dose.

(ii) *Indications for use.* Growth promotion and feed efficiency.

(iii) *Limitations.* For animals weighing 400 pounds or more; for subcutaneous ear implantation, one dose per animal.

(e) *NAS/NRC status.* These conditions of use are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety data.

[40 FR 13858, Mar. 27, 1975, as amended at 48 FR 48659, Oct. 20, 1983; 49 FR 13873, Apr. 9, 1984; 51 FR 21746, June 16, 1986; 52 FR 45312, Nov. 27, 1987; 53 FR 7406, Feb. 21, 1989]

§ 522.1962 Promazine hydrochloride injection.

(a) *Specifications.* Each milliliter of sterile aqueous solution contains 50 milligrams of promazine hydrochloride.

(b) *Sponsor.* In § 510.600(c) of this chapter, see No. 000008 for conditions of use as in paragraph (c)(1)(i) of this section; see No. 000856 for conditions of use as in paragraph (c)(1)(ii) of this section; see No. 000864 for conditions

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of use as in paragraph (c)(1)(iii) of this section.

(c) *Conditions of use.* (1)(i) To horses either intramuscularly or intravenously at a dosage of 0.2 to 0.5 milligram per pound of body weight, and to dogs and cats 1 to 3 milligrams per pound of body weight, every 4 to 6 hours as a tranquilizer or preanesthetic.¹

(ii) To horses either intramuscularly or intravenously at a dosage of 0.2 to 0.5 milligram per pound of body weight, and to dogs and cats at 1 to 2 milligrams per pound of body weight, every 4 to 6 hours as a tranquilizer, preanesthetic, for minor operative procedures in conjunction with local anesthesia, as adjunctive therapy for tetanus, and as an antiemetic in dogs and cats prior to worming, or to prevent motion sickness in dogs.¹

(iii) To horses intravenously at a dosage of 0.2 to 0.5 milligram per pound of body weight, as a tranquilizer and preanesthetic, as required.¹

(2) Not for use in conjunction with organophosphates because their toxicity may be potentiated, nor with procaine hydrochloride as its activity may be increased.¹

(3) Not for use in horses intended for food.¹

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

[46 FR 18962, Mar. 27, 1981]

§ 522.2002 Propiopromazine hydrochloride injection.

(a) *Chemical name.* 1-Propanone, 1-[10-[3-(dimethylamino) propyl] phenothiazine-2-yl]-, monohydrochloride.

(b) *Specifications.* Propiopromazine hydrochloride injection contains 5 or 10 milligrams of the drug in each milliliter of sterile aqueous solution.

(c) *Sponsor.* See No. 000033 in § 510.600(c) of this chapter.

(d) *Conditions of use.* (1) It is administered either intravenously or intramuscularly to dogs and cats for tran-

¹These conditions are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

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quillization at a dosage level of 0.05-0.5 milligram per pound of body weight and is also administered intravenously to dogs and cats as a preanesthetic at a dosage level of 0.25 milligram per pound of body weight.

(2) It is not to be used in conjunction with organophosphates and/or procaine hydrochloride since phenothiazines may potentiate the toxicity of organophosphates and the activity of procaine hydrochloride.

(3) For use only by or on the order of a licensed veterinarian.

[40 FR 13858, Mar. 27, 1975, as amended at 46 FR 60570, Dec. 11, 1981]

§ 522.2012 Prostalene solution.

(a) *Specifications.* Each milliliter of sterile solution contains 1 milligram of prostalene.

(b) *Sponsor.* No. 000033 in § 510.600(c) of this chapter.

(c) *Conditions of use—Horses.* (1) It is used in mares for the control of estrus.

(2) It is administered at a dose of 5 micrograms per kilogram of body weight as a single subcutaneous injection.

(3) Not for use in horses intended for food.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[41 FR 26854, June 30, 1976]

§ 522.2022 Protokylol hydrochloride injection.

(a) *Specifications.* Protokylol hydrochloride injection contains 0.5 milligram of protokylol hydrochloride per cubic centimeter of sterile aqueous solution.

(b) *Sponsor.* See No. 000859 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is used in dogs and cats for relief of bronchial spasm.¹

(2) It is administered subcutaneously or intramuscularly at a dosage level of 0.125 to 0.5 milligram to dogs and at a level of 0.125 to 0.25 milligram to cats.¹

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

§ 522.2063 Pyrilamine maleate injection.

(a) *Specifications.* The drug is a sterile aqueous solution with each milliliter containing 20 milligrams of pyrilamine maleate.

(b) *Sponsors.* See No. 000061 in § 510.600(c) of this chapter for uses in paragraph (c)(2)(i) of this section; see No. 000864 in § 510.600(c) of this chapter for uses in paragraph (c)(2)(ii) of this section.

(c) *Conditions of use.* (1) It is intended for treating horses in conditions in which antihistaminic therapy may be expected to lead to alleviation of some signs of disease.¹

(2)(i) It is administered intramuscularly, subcutaneously, or intravenously. Local injection at the site of insect bites may be indicated in severe cases. Intravenous injections must be given slowly to avoid symptoms of overdose. Dosage may be repeated every 6 to 12 hours whenever necessary. Horses, 40 to 60 milligrams per 100 pounds body weight; foals, 20 milligrams per 100 pounds body weight.¹

(ii) It is administered intravenously. Intravenous injections must be given slowly to avoid symptoms of overdose. Dosage may be repeated every 6 to 12 hours if necessary. Horses, 40 to 60 milligrams per 100 pounds body weight; foals, 20 milligrams per 100 pounds body weight.¹

(3) Do not use in horses intended for food purposes.¹

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

[40 FR 13858, Mar. 27, 1975; 41 FR 9150, Mar. 3, 1976, as amended at 42 FR 13549, Mar. 11, 1977; 42 FR 61256, Dec. 2, 1977; 51

FR 41477, Nov. 17, 1986; 52 FR 7832, Mar. 13, 1987; 54 FR 1164, Jan. 12, 1989]

§ 522.2100 Selenium, vitamin E injection.

(a)(1) *Specifications.* The drug is an emulsion containing in each milliliter, 5.48 milligrams sodium selenite (equivalent to 2.5 milligrams selenium), 50 milligrams of vitamin E (68 I.U.) (as d-alpha tocopheryl acetate), 250 milligrams polyoxyethylated vegetable oil, and 0.1 milligram thimerosal, and water for injection.

(2) *Sponsor.* See No. 000061 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) The drug is intended for use for the prevention and treatment of selenium-tocopherol deficiency syndrome in horses.

(ii) The drug is administered by intravenous or deep intramuscular injection in divided doses in 2 or more sites in the gluteal or cervical muscles at a dosage level of 1 milliliter per 100 pounds of body weight and may be repeated at 5 to 10 day intervals.

(iii) Do not use in horses intended for food.

(iv) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(b)(1) *Specifications.* The drug contains in each milliliter 2.19 milligrams of sodium selenite (equivalent to 1 milligram of selenium), 50 milligrams of vitamin E (68 I.U.) (as d-alpha tocopheryl acetate), 100 milligrams of polyoxyethylated vegetable oil, 1:10,000 thimerosal, and water for injection.

(2) *Sponsor.* See No. 000061 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) The drug is intended for use as an aid in alleviating and controlling inflammation, pain and lameness associated with certain arthropathies in dogs.

(ii) The drug is administered subcutaneously or intramuscularly in divided doses in 2 or more sites at a dosage level of 1 milliliter per 20 pounds of body weight with a minimum dosage of ¼ milliliter and a maximum dosage of 5 milliliters. The dosage is repeated at 3 day intervals until a satisfactory therapeutic response is observed. A maintenance regimen is then initiated which consists of 1 milliliter per 40 pounds of body weight with a minimum dosage of ¼ milliliter which is

¹ These conditions are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

¹ These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

repeated every 3 days or 7 days, or longer, as required to maintain continued improvement or an asymptomatic condition; or the drug may be used in capsule form for oral maintenance therapy.

(iii) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13858, Mar. 27, 1975, as amended at 52 FR 7832, Mar. 13, 1987]

§ 522.2120 Spectinomycin injection.

(a) *Specifications.* The spectinomycin dihydrochloride pentahydrate used in manufacturing the drug is the antibiotic substance produced by the growth of *Streptomyces flavopersicus* (var. Abbott) or the same antibiotic substance produced by any other means. Each milliliter of the drug contains the following amount of spectinomycin activity from spectinomycin dihydrochloride pentahydrate:

(1) 5 milligrams when used as provided in paragraph (d)(1) of this section.

(2) [Reserved]

(3) 100 milligrams when used as provided in paragraphs (d) (2), (3), and (4) of this section.

(b) *Sponsor.* See No. 000033 and No. 050604 in § 510.600(c) of this chapter.

(c) *Special considerations.* The quantity of spectinomycin referred to in this section refers to the equivalent weight of base activity for the drug.

(d) *Conditions of use.* It is administered as spectinomycin dihydrochloride pentahydrate as follows:

(1) Subcutaneously in the treatment of 1-to-3-day-old turkey poults at the rate of 1 to 2 milligrams per poult as an aid in the prevention of mortality associated with Arizona group infection.

(2) Subcutaneously in the treatment of 1-to-3-day old:

(i) Turkey poults at the rate of 5 milligrams per poult as an aid in the control of chronic respiratory disease (CRD) associated with *E. coli*.

(ii) Baby chicks at the rate of 2.5 to 5 milligrams per chick as an aid in the control of mortality and to lessen severity of infections caused by *M. synoviae*, *S. typhimurium*, *S. infantis*, and *E. coli*.

(3) Intramuscularly in the treatment of dogs:

(i) At a dosage level of 2.5 milligrams to 5.0 milligrams per pound of body weight twice daily. Treatment may be continued for 4 days. For treatment of infections caused by gram-negative and gram-positive organisms susceptible to spectinomycin.

(ii) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(4) Administer single injection of 0.1 milliliter (10 milligrams) subcutaneously in nape of neck of 1- to 3-day-old turkey poults as an aid in control of airsacculitis associated with *M. meleagridis* sensitive to spectinomycin.

[40 FR 13858, Mar. 27, 1975, as amended at 43 FR 9273, Mar. 7, 1978; 46 FR 18964, Mar. 27, 1981; 47 FR 14149, Apr. 2, 1982]

§ 522.2150 Stanazolol sterile suspension.

(a) *Specifications.* Each milliliter of sterile suspension contains 50 milligrams of stanozolol.

(b) *Sponsor.* No. 000934 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) Used as an anabolic steroid treatment in dogs, cats, and horses.

(2) Administered to dogs and cats by deep intramuscular injection in the thigh at weekly intervals, for several weeks. For cats and small breeds of dogs, 25 milligrams. For larger dogs, 50 milligrams.

(3) Administered to horses by deep intramuscular injection in the gluteal region at weekly intervals, for not more than 4 weeks; 25 milligrams per 100 pounds of body weight.

(4) Not for use in horses intended for food.

(5) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 46101, Oct. 6, 1975, as amended at 43 FR 36995, July 19, 1977]

§ 522.2200 Sulfachlorpyridazine.

(a) *Chemical name.* N¹-(6-Chloro-3-pyridazinyl) sulfanilamide.

(b) *Specifications.* Melting point range 190° C to 191° C.

(c) *Sponsor.* See No. 053501 in § 510.600(c) of this chapter.

(d) *Related tolerances.* See § 556.630 of this chapter.

(e) *Conditions of use.* It is used for injection into calves as follows:

(1) *Amount.* 30 to 45 milligrams per pound of body weight per day.

(2) *Indications for use.* Treatment of diarrhea caused or complicated by *E. coli* (colibacillosis).

(3) *Limitations.* Administer as the sodium salt of sulfachlorpyridazine intravenously in aqueous solution for 1 to 5 days in divided doses twice daily; treated calves must not be slaughtered for food during treatment or for 5 days after the last treatment.

[40 FR 13658, Mar. 27, 1975, as amended at 50 FR 41489, Oct. 11, 1985]

§ 522.2220 Sulfadimethoxine injection.

(a)(1) *Specifications.* Sulfadimethoxine injection containing 400 milligrams per milliliter.

(2) *Sponsor.* See No. 000004 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) It is used or intended for use in dogs and cats as follows:

(a) For the treatment of respiratory, genitourinary tract, enteric, and soft tissue infections when caused by *Streptococci*, *Staphylococci*, *Escherichia*, *Salmonella*, *Klebsiella*, *Proteus*, or *Shigella* organisms sensitive to sulfadimethoxine, and in the treatment of canine bacterial enteritis associated with coccidiosis and canine *Salmonellosis*.

(b) It is administered by intravenous or subcutaneous injection at an initial dose of 55 milligrams per kilogram of body weight followed by 27.5 milligrams per kilogram of body weight every 24 hours.

(c) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(ii) It is used or intended for use in horses as follows:

(a) For the treatment of respiratory disease caused by *Streptococcus equi* (strangles).

(b) It is administered by intravenous injection at an initial dose of 55 milligrams per kilogram of body weight followed by 27.5 milligrams per kilogram of body weight every 24 hours until the patient is asymptomatic for 48 hours.

(c) Not for use in horses intended for food.

(d) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(iii) It is used or intended for use in cattle as follows:

(a) For the treatment of shipping fever complex, bacterial pneumonia, calf diphtheria, and foot-rot.

(b) It is administered by intravenous injection at an initial dose of 25 milligrams per pound of body weight followed by 12.5 milligrams per pound of body weight every 24 hours until the animal is asymptomatic for 48 hours.

(c) Milk taken from animals during treatment and for 60 hours (5 milkings) after the latest treatment must not be used for food. Do not administer within 5 days of slaughter.

(d) Tissue damage may result from perivascular infiltration.

(b) [Reserved]

(c)(1) *Specifications.* Sulfadimethoxine containing 100 milligrams per milliliter.

(2) *Sponsor.* See No. 011716 in § 510.600(c) of this chapter for use in dogs, cats, and horses; see No. 054273 in § 510.600(c) of this chapter for use in dogs.

(3) *Conditions of use.* (i) It is used or intended for use in the treatment of sulfadimethoxine-susceptible bacterial infections in dogs, cats and horses.

(ii) It is administered by subcutaneous, intramuscular or intravenous injection to dogs and cats and by intravenous injection only to horses at an initial dose of 25 milligrams per pound of body weight followed by 12.5 milligrams per pound of body weight every 24 hours thereafter. Continue treatment until the animal is free from symptoms for 48 hours.

(iii) Not to be administered to horses intended for use as food.

(iv) For use by or on the order of a licensed veterinarian.

(d) *Related tolerances.* See § 556.640 of this chapter.

[40 FR 13658, Mar. 27, 1975, as amended at 40 FR 34112, Aug. 14, 1975; 40 FR 42007, Sept. 10, 1975; 50 FR 254, Jan. 3, 1985; 53 FR 40728, Oct. 18, 1988]

§ 522.2240 Sulfaethoxypyridazine.

(a) *Chemical name.* *N*¹-(6-Ethoxy-3-pyridazinyl) sulfanilamide.

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(b) *Specifications.* Melting point range of 180° C to 186° C.

(c) *Sponsor.* See No. 010042 in § 510.600(c) of this chapter.

(d) *Related tolerances.* See § 556.650 of this chapter.

(e) *Conditions of use.* It is used for injection into cattle as follows:

(1) *Amount.* 2.5 grams per 100 pounds of body weight per day.

(2) *Indications for use.* Treatment of respiratory infection (pneumonia, shipping fever), foot rot, calf scours; as adjunctive therapy in septicemia accompanying mastitis and metritis.

(3) *Limitations.* Administer intravenously for not more than 4 days; or first treatment may be followed by 3 days of treatment with sulfaethoxypyridazine in drinking water, feed, or tablet in accordance with § 558.579(e) or §§ 520.2240a(e) and 520.2240b(e) of this chapter; as sodium sulfaethoxypyridazine; do not treat within 16 days of slaughter; as sole source of sulfonamide; milk that has been taken from animals during treatment and for 72 hours (6 milkings) after the latest treatment must not be used for food; for use by or on the order of a licensed veterinarian.

[40 FR 13858, Mar. 27, 1975, as amended at 41 FR 11011, Mar. 15, 1976]

§ 522.2260 Sulfamethazine injectable solution.

(a) *Specifications.* Each milliliter of sterile aqueous solution contains 250 milligrams of sulfamethazine sodium.

(b) *Sponsor.* See No. 010042 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See § 556.670 of this chapter.

(d) *NAS/NRC status.* The conditions of use are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(e) *Conditions of use—(1) Amount.* 20 milliliters for each 50 pounds of body weight (100 milligrams per pound) initially, 20 milliliters per 100 pounds of body weight (50 milligrams per pound) daily thereafter for cattle.

(2) *Indications for use.* For cattle for treatment of bacterial pneumonia and bovine respiratory disease complex

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(shipping fever complex) (*Pasteurella* spp.), colibacillosis (bacterial scours) (*Escherichia coli*), necrotic pododermatitis (foot rot) (*Fusobacterium necrophorum*), calf diphtheria (*Fusobacterium necrophorum*), acute mastitis and acute metritis (*Streptococcus* spp.) when caused by one or more pathogenic organisms sensitive to sulfamethazine.

(3) *Limitations.* For intravenous use only. Not for use in lactating dairy animals. Withdraw medication from cattle 10 days prior to slaughter for food. If symptoms persist for 2 or 3 days, consult a veterinarian. Adequate water intake is important for animals treated with sulfonamides. Treatment should continue 24 to 48 hours beyond the remission of disease symptoms, but not to exceed a total of 5 consecutive days.

[46 FR 62055, Dec. 22, 1981]

§ 522.2340 Sulfomyxin.

(a) *Specifications.* Sulfomyxin for injection is sterile. It is derived from the antibiotic substance produced by the growth of *Bacillus polymyxa* or is the same substance produced by any other means.

(b) *Sponsor.* See No. 000069 in § 510.600(c) of this chapter.

(c) *Special considerations.* The quantities of antibiotic in paragraph (e) of this section refer to the activity of the appropriate standard.

(d) *Related tolerances.* See § 556.700 of this chapter.

(e) *Conditions of use.* (1) It is used or intended for use in chickens and turkeys as an aid in the treatment of disease caused or complicated by *E. coli*, such as colibacillosis and complicated chronic respiratory disease.

(2) It is administered by subcutaneous injection as follows:

Age of birds in days	Antibiotic activity	
	Chickens (units)	Turkeys (units)
1 to 14.....	12,500	12,500
15 to 28.....	25,000	25,000
29 to 63.....	50,000	50,000
Over 63.....	50,000	100,000

(3) A second injection may be given 3 days later if symptoms persist.

(4) Not for use in laying hens; do not treat chickens within 5 days of slaughter; do not treat turkeys within 7 days of slaughter.

522.2404 Thalbarbitone sodium for injection.

(a) *Specifications.* Thalbarbitone sodium for injection when reconstituted with sterile distilled water provides 4 milligrams of thalbarbitone sodium per milliliter of solution.

(b) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is administered as a general anesthetic for surgical procedures on dogs, cats, swine, sheep, cattle, and horses. The drug is used for procedures of relative short duration. However, the period of anesthesia can be lengthened by a lower initial injection and supplemental administration during surgery.

(2) It is administered intravenously. The drug is injected slowly to dogs, cats, cattle, sheep, and swine. For horses, it is recommended that a pre-anesthetic sedation be administered to the horse 30 minutes before the drug is administered. The drug is then injected rapidly and completely. The drug is used at the following dosage levels:

Species	Weight of animal in pounds	Dosage in milligrams per pound
Do.....	Over 50.....	14.1
Do.....	30-50.....	18.8
Do.....	10-30.....	23.5
Do.....	Under 10.....	28.2
Do.....	31.3-37.6.....	31.3-37.6
Do.....	6.3-7.8.....	6.3-7.8
Do.....	8.7-9.4.....	8.7-9.4
Do.....	9.4-11.8.....	9.4-11.8

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

522.2424 Sodium thiamylal for injection.

(a) *Specifications.* The drug is a sterile dry powder. It is reconstituted aseptically with sterile distilled water, water for injection, or sodium chloride injection, to a desired concentration of 1 to 4 percent sodium thiamylal.

(b) *Sponsors.* See code Nos. 000010, 000856, and 054273 in § 510.500(c) of this chapter.

(c) *Conditions of use.* (1) It is used as an ultra-short-acting anesthetic in dogs, cats, swine, horses, and cattle.

(2) When diluted aseptically to the desired concentration and administered intravenously to effect, the average single dose is:

(i) Dogs and cats: 8 milligrams per pound of body weight (when used with a preanesthetic, generally one-half the normal dose).

(ii) Swine: 40 milligrams per 5 pounds of body weight.

(iii) Horses: Light anesthesia, 1 gram per 500 pounds to 1,100 pounds of body weight; deep anesthesia, 1 gram per 300 pounds of body weight (40 milligrams per 12 pounds of body weight).

(iv) Cattle: Short duration, 20 milligrams per 5 pounds of body weight; longer duration, 40 milligrams per 7 pounds of body weight.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(4) *NAS/NRC status:* The conditions of use specified in this paragraph are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified in § 514.111 of this chapter, but may require bioequivalency and safety information.

[40 FR 25812, June 19, 1975, as amended at 49 FR 8434, Mar. 7, 1984; 53 FR 23390, June 22, 1988; 53 FR 40728, Oct. 18, 1988]

§ 522.2444 Sodium thiopental implantation or injectable dosage forms.

§ 522.2444a Sodium thiopental for injection.

(a) *Specifications.* The drug contains sodium thiopental sterile powder for dilution with sterile water for injection.

(b) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is used as an anesthetic for intravenous administration to dogs and cats during short to moderately long surgical and other procedures. It is also used to induce anesthesia in dogs and cats which

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then have surgical anesthesia maintained by use of a volatile anesthetic.

(2) It is administered as follows:

(i) For brief anesthesia (6 to 10 minutes) a dosage of 6 to 9 milligrams per pound of body weight is suggested.

(ii) To obtain anesthesia of 15 to 25 minutes duration the suggested dosage is 10 to 12 milligrams per pound of body weight.

(iii) Use of a preanesthetic tranquilizer or morphine will decrease the dosage of sodium thiopental required, provide for smoother induction and smoother recovery, and sometimes prolong the recovery period. If morphine is used as a preanesthetic agent the dose of the barbiturate can be reduced as much as 40 to 50 percent. When a tranquilizer is administered the barbiturate dosage can be reduced 10 to 25 percent.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

§ 522.2444b Sodium thiopental, sodium pentobarbital for injection.

(a) *Specifications.* Each gram of the drug contains 750 milligrams of sodium thiopental and 250 milligrams of sodium pentobarbital sterile powder for dilution with sterile water for injection.

(b) *Sponsor.* See No. 050604 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is used as an anesthetic for intravenous administration to dogs and cats during short to moderately long surgical procedures.

(2) It is administered as follows:

(i) For total anesthesia, it is given at approximately 10 to 12 milligrams per pound of body weight over a period of 3.5 to 5 minutes.

(ii) When preanesthetic medication is used, it is important to wait at least an hour before administering thiopental and sodium pentobarbital for injection, and the dosage necessary for anesthesia is reduced. Usually $\frac{1}{2}$ to $\frac{3}{4}$ the normal amount is adequate.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13858, Mar. 27, 1975, as amended at 47 FR 14149, Apr. 2, 1982]

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§ 522.2470 Tiletamine hydrochloride and zolazepam hydrochloride for injection.

(a) *Specifications.* Tiletamine hydrochloride and zolazepam hydrochloride for injection when reconstituted with sterile distilled water provides tiletamine hydrochloride and zolazepam hydrochloride equivalent to 50 milligrams of tiletamine base and 50 milligrams of zolazepam base per milliliter of solution.

(b) *Sponsor.* See No. 000031 in § 510.600(c) of this chapter.

(c) *Conditions of use.*—(1) *Indications for use.* It is used for restraint or for anesthesia combined with muscle relaxation in cats and in dogs for restraint and minor procedures of short duration (30 minutes) requiring mild to moderate analgesia.

(2) *Amount.* Expressed as milligrams of the drug combination:

(i) In healthy dogs: An initial intramuscular dosage of 3 to 4.5 milligrams per pound of body weight for diagnostic purposes; 4.5 to 6 milligrams per pound of body weight for minor procedures of short duration such as repair of lacerations and wounds, castrations, and other procedures requiring mild to moderate analgesia. Supplemental doses when required should be less than the initial dose and the total dose given should not exceed 12 milligrams per pound of body weight. The maximum total safe dose is 13.6 milligrams per pound of body weight.

(ii) In healthy cats: An initial intramuscular dosage of 4.4 to 5.4 milligrams per pound of body weight is recommended for such procedures as dentistry, treatment of abscesses, foreign body removal, and related types of surgery; 4.8 to 5.7 milligrams per pound of body weight for minor procedures requiring mild to moderate analgesia, such as repair of lacerations, castrations, and other procedures of short duration. Initial dosages of 6.5 to 7.2 milligrams per pound of body weight are recommended for ovariohysterectomy and onychectomy. When supplemental doses are required, such individual supplemental doses should be given in increments that are less than the initial dose and the total dose given (initial dose plus supplemental doses) should not exceed

the maximum allowable safe dose of 32.7 milligrams per pound of body weight.

(3) *Limitations.* Discard unused reconstituted solution after 48 hours. Not for use in dogs and cats with pancreatic disease, or with severe cardiac or pulmonary dysfunction. Not for use in pregnant animals. Not for use in cats suffering with renal insufficiency. The dosage should be reduced in geriatric dogs and cats. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[47 FR 15328, Apr. 9, 1982, as amended at 51 FR 24142, July 2, 1986]

§ 522.2476 Trenbolone acetate.

(a) *Specifications.* Each pellet for implanting contains 20 milligrams of trenbolone acetate.

(b) *Sponsor.* See 012579 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See § 556.739 of this chapter.

(d) *Conditions of use—(1) Heifers* 200 milligrams trenbolone acetate (10 pellets of 20 milligrams each) for increased rate of weight gain and improved feed efficiency in growing-finishing feedlot heifers, use last 63 days prior to slaughter.

(2) *Steers.* 140 milligrams trenbolone acetate (7 pellets of 20 milligrams each) for improved feed efficiency in growing-finishing feedlot steers, use 126 days prior to slaughter, should be reimplanted once after 63 days.

(3) *Limitations.* Not for use in animals intended for subsequent breeding or in dairy animals. Implant in ear only.

[52 FR 24995, July 2, 1987]

§ 522.2480 Triamcinolone injection.

(a) *Chemical name.* 9-Fluoro-11 β ,16 α ,17,21-tetrahydroxypregna-1,4-diene-3,20-dione.

(b) *Specifications.* Each cubic centimeter of triamcinolone injection contains 2.5 milligrams of triamcinolone and 10 milligrams of procaine hydrochloride with 0.1 percent of sodium bisulfite and 84.4 percent of polyethylene glycol 400.

(c) *Sponsor.* See No. 000859 in § 510.600(c) of this chapter.

(d) *Conditions of use.* (1) The drug is indicated for use in dogs and cats for its anti-inflammatory activity.¹

(2)(i) In dogs, the drug may be given by intramuscular or subcutaneous injection at 0.625 milligram for each 10 pounds of body weight, and, if only one or two injections are anticipated, the dosage may be doubled. It may also be given to dogs by intra-articular administration at from 0.625 milligram to 1.25 milligrams per dose. Repeat dosage as indicated.¹

(ii) In cats, the drug may be given by intramuscular or subcutaneous injection at 0.625 milligram for each 10 pounds of body weight. It may also be given by intra-articular administration at from 0.31 milligram to 0.625 milligram per dose. Repeat dosage as indicated.¹

(iii) Since requirements vary with the individual animal, recommended dosage is approximate and must be adjusted to the response of the individual animal. Generally, initial dosages are at a higher range. When response is satisfactory, gradually reduce dosage until a minimum dose is obtained. This is particularly important for long-term medication. If additional treatment or a long-term treatment is necessary, triamcinolone tablets may be used as a maintenance dosage.¹

(3) For use by or on the order of a licensed veterinarian.¹

[40 FR 13858, Mar. 27, 1975, as amended at 47 FR 14150, Apr. 2, 1982]

§ 522.2483 Sterile triamcinolone acetonide suspension.

(a) *Specifications.* Each milliliter of suspension contains 2 or 6 milligrams triamcinolone acetonide.

(b) *Sponsor.* See 053501 and 054273 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount—(i) Dogs and cats—(a) Intramuscular or subcutaneous.* Single injection of 0.05 to 0.1 milligram (mg.) per pound of body weight in inflammatory, ar-

¹ These conditions are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

thritic, or allergic disorders. Single injection of 0.1 mg. per pound of body weight in dermatologic disorders. If symptoms recur, the dose may be repeated, or oral corticosteroid therapy may be instituted.¹

(b) *Intralesional.* 1.2 to 1.8 mg., divided in several injections, spaced around the lesion at 0.5 to 2.5 centimeters apart depending on the size. At any one site the dose injected should not exceed 0.6 mg. and should be well into the cutis to prevent rupture of the epidermis. When treating animals with multiple lesions, do not exceed a total dose of 6 mg.

(c) *Intra-articular and intrasynovial.* Single injection of 1 to 3 mg. dose, dependent on size of joint and severity of symptoms. After 3 or 4 days, repeat dosage if indicated. If initial results are inadequate or too transient, dosage may be increased, not to exceed 3 mg.

(ii) *Horses—(a) Intramuscular or subcutaneous.* Single injection of 0.01 to 0.02 mg. per pound of body weight. Usual dose, 12 to 20 mg.

(b) *Intra-articular and intrasynovial.* Single injection of 6 to 18 mg. dose, dependent on size of joint and severity of symptoms. After 3 or 4 days, repeat dosage if indicated. If initial results are inadequate or too transient, dosage may be increased, not to exceed 18 mg.

(2) *Indications for use.* Treatment of inflammation and related disorders in dogs, cats, and horses;¹ and management and treatment of acute arthritis and allergic and dermatologic disorders in dogs and cats.

(3) *Limitations.* (i) Do not use in viral infections. With bacterial infections, appropriate antibacterial therapy should be used.

(ii) Do not use in animals with tuberculosis, chronic nephritis, or cushingoid syndrome, except for emergency therapy.

(iii) Not for use in horses intended for food.

¹ These conditions are NAS/NRC reviewed and are deemed effective. Applications for these uses need not include the effectiveness data specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(iv) Clinical and experimental data have demonstrated that corticosteroids administered orally or parenterally to animals may induce the first stage of parturition when administered during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis.

(v) Do not use in the treatment of laminitis.

(vi) Intra-articular injection in equine leg injuries may produce osseous metaplasia.

(vii) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[43 FR 4976, Feb. 7, 1978, as amended at 50 FR 41490, Oct. 11, 1985; 52 FR 1903, Jan. 14, 1987; 53 FR 40728, Oct. 18, 1988]

§ 522.2582 Triflupromazine hydrochloride injection.

(a) *Specifications.* Triflupromazine hydrochloride injection contains 20 milligrams of triflupromazine hydrochloride in each milliliter of sterile aqueous solution.

(b) *Sponsor.* See No. 053501 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used in dogs, cats, and horses to relieve anxiety and to help control psychomotor overactivity as well as to increase the tolerance of animals to pain and pruritus. The drug is indicated in various office and clinical procedures which require the aid of a tranquilizer, antiemetic, or preanesthetic.¹

(2) The drug is administered to dogs either intravenously at a dosage level of 0.5 to 1 milligram per pound of body weight daily, or intramuscularly at a dosage level of 1 to 2 milligrams per pound of body weight daily. It is administered to cats intramuscularly at a dosage level of 2 to 4 milligrams per pound of body weight daily. It is administered to horses intravenously or intramuscularly at a dosage level of 10 to 15 milligrams per 100 pounds of body weight daily to a maximum dose of 100 milligrams.¹

(3) Not for use in horses intended for food.¹

(4) Do not use in conjunction with organophosphates and/or procaine hydrochloride, because phenothiazines

may potentiate the toxicity of organophosphates and the activity of procaine hydrochloride.¹

(5) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

[40 FR 13858, Mar. 27, 1975, as amended at 50 FR 41490, Oct. 11, 1985]

§ 522.2610 Trimethoprim and sulfadiazine sterile suspension.

(a)(1) *Specifications.* Each milliliter of sterile aqueous suspension contains 240 milligrams (40 milligrams of trimethoprim and 200 milligrams of sulfadiazine).

(2) *Sponsor.* See 000033 and 017220 in § 510.600(c) of this chapter.

(3) *Conditions of use—(i) Dosage.* One milliliter (40 milligrams of trimethoprim and 200 milligrams of sulfadiazine) per 20 pounds (9 kilograms) of body weight per day.

(ii) *Indications.* For dogs for treatment of acute urinary tract infections, acute bacterial complications of distemper, acute respiratory tract infections, acute alimentary tract infections, and acute septicemia due to *Streptococcus zooepidemicus*.

(iii) *Limitations.* For subcutaneous use in dogs only; administer once every 24 hours, or for severe infections, after an initial dose, administer half the normal daily dose every 12 hours; continue therapy 2 to 3 days after clinical signs of infection have subsided; if no improvement is seen in 3 to 5 days, reevaluate diagnosis; injection may be used alone or in conjunction with oral dosing; not recommended for use for more than 14 days; a complete blood count should be done for prolonged use; Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(b)(1) *Specifications.* Each milliliter of sterile aqueous suspension contains 180 milligrams (80 milligrams of trimethoprim and 400 milligrams of sulfadiazine (as the sodium salt)).

(2) *Sponsor.* See 000033 and 017220 in § 510.600(c) of this chapter.

(3) *Conditions of use—(i) Dosage.* Two milliliters (180 milligrams of trimethoprim and 800 milligrams of sulfadiazine) per 100 pounds (45 kilograms) of body weight per day.

(ii) *Indications.* For horses where systemic anti-bacterial action against sensitive organisms is required during treatment of acute strangles, respiratory tract infections, acute urogenital infections, and wound infections and abscesses.

(iii) *Limitations.* For intravenous use; administer as single, daily dose for 5 to 7 days; daily dose may also be halved and given morning and evening; continue acute infection therapy 2 to 3 days after clinical signs have subsided; if no improvement of acute infections is seen in 3 to 5 days, reevaluate diagnosis; a complete blood count should be done periodically for prolonged use; not for use in horses intended for food; Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[48 FR 241, Jan. 4, 1983, as amended at 48 FR 23180, May 24, 1983; 48 FR 42809, Sept. 20, 1983]

§ 522.2615 Tripeleminamine hydrochloride injection.

(a) *Specifications.* Each milliliter of aqueous solution contains 20 milligrams of tripeleminamine hydrochloride.

(b) *Sponsor.* See No. 053501 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount—(i) Dogs, cats, and horses.* For intramuscular use only at a dose of 0.5 milligram per pound of body weight.

(ii) *Cattle.* Administer intravenously or intramuscularly at a dose of 0.5 milligram per pound of body weight.

(2) *Indications for use.* For use in treating conditions in which antihistaminic therapy may be expected to lead to alleviation of some signs of disease.

(3) *Limitations.* Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(d) *NAS/NRC status.* These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety data.

[51 FR 44450, Dec. 10, 1986]

§ 522.2640a

§ 522.2640 Tylosin injectable dosage forms.

§ 522.2640a Tylosin injection.

(a) *Specifications.* Each milliliter of sterile solution of 50 percent propylene glycol with 4 percent benzyl alcohol contains 50 to 200 milligrams of tylosin activity (as tylosin base). Tylosin conforms to the appropriate antibiotic standard. Tylosin contains at least 95 percent tylosin as a combination of tylosin A, tylosin B, tylosin C, and tylosin D of which at least 80 percent is tylosin A as determined by a method entitled "Determination of Factor Content in Tylosin by High Performance Liquid Chromatography," which is incorporated by reference. Copies are available from the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857, or available for inspection at the Office of the Federal Register, 1100 L St. NW., Washington, DC 20408.

(b) *Sponsors.* (1) See No. 000986 in § 510.600(c) of this chapter for use in paragraphs (e)(1), (2), and (3) of this section.

(2) See No. 054273 in § 510.600(c) of this chapter for use as in paragraphs (e)(1) and (2) of this section.

(c) *NAS/NRC status.* These conditions of use are NAS/NRC reviewed and found effective. NADA's for these uses need not include effectiveness data as specified by § 514.111 of this chapter but may require bioequivalency and safety information.

(d) *Related tolerances.* See § 556.740 of this chapter.

(e) *Conditions of use—(1) Beef cattle and nonlactating dairy cattle—(i) Amount.* 8 milligrams per pound of body weight once daily.

(ii) *Indications for use.* Treatment of bovine respiratory complex (shipping fever, pneumonia) usually associated with *Pasteurella multocida* and *Corynebacterium pyogenes*; foot rot (necrotic pododermatitis) and calf diphtheria caused by *Fusobacterium necrophorum* and metritis caused by *Corynebacterium pyogenes*.

(iii) *Limitations.* Administer intramuscularly for not more than 5 consecutive days. Continue treatment 24 hours after symptoms disappear. Do

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not inject more than 10 milliliters per site. Do not use in lactating dairy cattle. Use a 50-milligram-per-milliliter solution for calves weighing less than 200 pounds. Do not administer within 21 days of slaughter.

(2) *Swine—(i) Amount.* 4 milligrams per pound of body weight twice daily.

(ii) *Indications for use.* Treatment of swine arthritis caused by *Mycoplasma hyosynoviae*; swine pneumonia caused by *Pasteurella* spp.; swine erysipelas caused by *Erysipelothrix rhusiopathiae*; swine dysentery associated with *Treponema hyodysenteriae* when followed by appropriate medication in the drinking water and/or feed.

(iii) *Limitations.* Administer intramuscularly for not more than 3 consecutive days. Continue treatment 24 hours after symptoms disappear. Do not inject more than 5 milliliters per site. Do not administer within 14 days of slaughter. If tylosin medicated drinking water is used as followup treatment for swine dysentery, the animal should thereafter receive feed containing 40 to 100 grams of tylosin per ton for 2 weeks to assure depletion of tissue residues.

(3) *Dogs and cats—(i) Amount.* 3 to 5 milligrams per pound of body weight at 12- to 24-hour intervals.

(ii) *Indications for use—(a) Dogs.* Treatment of upper respiratory infections such as bronchitis, tracheobronchitis, tracheitis, laryngitis, tonsillitis, and pneumonia caused by *Staphylococci* spp., hemolytic *Streptococci* spp., and *Pasteurella multocida*.

(b) *Cats.* Treatment of upper respiratory infections when caused by *Staphylococci* spp. and hemolytic *Streptococci* spp. and for feline pneumonitis when caused by tylosin susceptible organisms.

(iii) *Limitations.* For intramuscular use only. If there is no response to therapy in 5 days, diagnosis and treatment should be reassessed. Use a 50-milligram-per-milliliter solution only. Dogs and cats receiving a dose of less than 50 milligrams (1 milliliter) should be dosed with a tuberculin syringe. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[46 FR 48643, Oct. 2, 1981, as amended at 47 FR 9398, Mar. 5, 1982; 50 FR 49841, Dec. 5, 1985; 50 FR 50292, Dec. 10, 1985; 53 FR 40728, Oct. 18, 1988]

§ 522.2640b Tylosin tartrate for injection.

(a) *Specifications.* The drug is a sterile powder containing a mixture of tylosin tartrate and sodium citrate which is reconstituted to provide 25 milligrams of tylosin activity per milliliter. Tylosin as the tartrate salt, conforms to the appropriate antibiotic standard. Tylosin contains at least 95 percent tylosin as a combination of tylosin A, tylosin B, tylosin C, and tylosin D of which at least 80 percent is tylosin A as determined by a method entitled "Determination of Factor Content in Tylosin by High Performance Liquid Chromatography," which is incorporated by reference. Copies are available from the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857, or available for inspection at the Office of the Federal Register, 1100 L St. NW., Washington, DC 20408.

(b) *Sponsor.* See No. 000986 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See § 556.740 of this chapter.

(d) *Conditions of use—(1) Chickens—*
(i) *Amount.* 25 milligrams per 2 pounds of body weight.

(ii) *Indications for use.* As an aid in the control and treatment of chronic respiratory disease caused by *Mycoplasma gallisepticum* sensitive to tylosin.

(iii) *Limitations.* Not for use in laying chickens producing eggs for human consumption; inject under the loose skin of the neck behind the head; if no improvement is noted within 5 days, diagnosis should be re-evaluated; do not treat within 3 days of slaughter.

(2) *Turkeys—(i) Amount.* 6.25 to 12.5 milligrams per sinus.

(ii) *Indications for use.* As an aid in the control and treatment of infectious sinusitis caused by *Mycoplasma gallisepticum* sensitive to tylosin.

(iii) *Limitations.* Do not use in laying turkeys producing eggs for human consumption; inject 6.25 milligrams to 12.5 milligrams per sinus depending on severity of condition; treat-

ment may be repeated in 10 days if the swelling persists; do not treat within 5 days of slaughter; may be used in conjunction with tylosin in drinking water as indicated in § 520.2640(e)(2) of this chapter.

[46 FR 48643, Oct. 2, 1981, as amended at 50 FR 49841, Dec. 5, 1985; 50 FR 49841, Dec. 5, 1985]

§ 522.2662 Xylazine hydrochloride injection.

(a) *Specifications.* Xylazine hydrochloride injection is a sterile aqueous solution containing xylazine hydrochloride equivalent to 100 milligrams of xylazine in each milliliter of solution when intended for use in horses, wild deer, and elk, and 20 milligrams of xylazine per milliliter of solution when intended for use in dogs and cats.

(b) *Sponsor.* See No. 000859 in § 510.600(c) of this chapter for use in horses, wild deer, elk, dogs, and cats. See Nos. 032998 and 054273 in § 510.600(c) of this chapter for use in horses only.

(c) *Conditions of use.* (1) The drug is used in horses, wild deer, elk, dogs, and cats to produce sedation, as an analgesic, and a preanesthetic to local anesthesia. It may also be used in horses, dogs, and cats as a preanesthetic to general anesthesia.

(2) It is administered as follows:

(i) To horses from a solution containing 100 milligrams of xylazine per milliliter, intravenously at 0.5 milligram per pound of body weight, or intramuscularly at 1.0 milligram per pound of body weight.

(ii) To dogs and cats from a solution containing 20 milligrams of xylazine per milliliter; intravenously at 0.5 milligram per pound of body weight or intramuscularly or subcutaneously at 1.0 milligram per pound of body weight. In dogs over 50 pounds, a dosage of 0.5 mg. per pound administered intramuscularly may provide sufficient sedation and/or analgesia for most procedures.

(iii) To wild deer and elk from a solution containing 100 milligrams of xylazine (as xylazine hydrochloride) per milliliter, intramuscularly, by hand syringe or syringe dart, in the heavy

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muscles of the croup or shoulder as follows:

(a) Fallow deer, 2 to 4 milligrams per pound.

(b) Mule deer, sika deer, and white-deer, 1 to 2 milligrams per pound.

(c) Elk, 0.25 to 0.5 milligram per pound.

(3) Not to be administered to food-producing animals.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13858, Mar. 27, 1975, as amended at 41 FR 24884, June 21, 1976; 41 FR 26265, July 9, 1976; 53 FR 4848, Feb. 18, 1988; 53 FR 23608, June 23, 1988; 53 FR 40728, Oct. 18, 1988]

§ 522.2680 Zeranol.

(a) *Chemical name.* 6-(6,10-Dihydroxyundecyl)-β-resorcylic acid-μ-lactone (C₂₂H₃₆O₆).

(b) *Specifications.* (1) Melting point range 181°-185° C.

(2) Ultraviolet absorbance: A solution of zeranol in methanol having a concentration of 10 micrograms per milliliter exhibits three maxima at approximately 218, 265, and 304μ.

(c) *Sponsor.* See No. 011716 in § 510.600(c) of this chapter.

(d) [Reserved]

(e) *Related tolerances.* See § 556.760 of this chapter.

(f) *Conditions of use.* It is used for subcutaneous ear implantation in animals as follows:

(1) *Beef cattle*—(i) *Amount.* Three 12-milligram implants per dose.

(ii) *Indications for use.* For increased rate of weight gain and improved feed conversion.

(iii) *Limitations.* For beef cattle (including weaned beef calves, growing beef cattle, feedlot steers, and feedlot heifers); do not implant animals within 65 days of slaughter.

(2) *Feedlot lambs*—(i) *Amount.* One 12-milligram implant per dose.

(ii) *Indications for use.* For increased rate of weight gain and improved feed conversion.

(iii) *Limitations.* Do not implant animals within 40 days of slaughter.

(3) *Suckling beef calves*—(i) *Amount.* Three 12-milligram implants per dose.

(ii) *Indications for use.* For increased rate of weight gain.

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(iii) *Limitations.* Do not implant animals within 65 days of slaughter.

[40 FR 13858, Mar. 27, 1975, as amended at 53 FR 20843, June 7, 1988; 53 FR 23340, June 21, 1988]

PART 524—OPHTHALMIC AND TOPICAL DOSAGE FORM NEW ANIMAL DRUGS NOT SUBJECT TO CERTIFICATION

Sec.

524.86 Amitraz liquid.

524.321 Cephalonium, polymyxin B sulfate, flumethasone, iodochlorhydroxyquin, piperocaine hydrochloride topical ointment.

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524.680a Dimethyl sulfoxide solution.

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524.900 Famphur.

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524.980 Flumethasone, neomycin sulfate, and polymyxin B sulfate ophthalmic solution.

524.981 Fluocinolone acetonide ophthalmic and topical dosage forms.

524.981a Fluocinolone acetonide cream.

524.981b Fluocinolone acetonide solution.

524.981c Fluocinolone acetonide, neomycin sulfate cream.

524.981d Fluocinolone acetonide, dimethyl sulfoxide solution.

524.981e Fluocinolone acetonide, dimethyl sulfoxide otic solution.

524.1005 Furazolidone aerosol powder.

524.1044 Gentamicin sulfate ophthalmic and topical dosage forms.

524.1044a Gentamicin ophthalmic solution.

524.1044b Gentamicin sulfate, betamethasone valerate otic solution.

524.1044c Gentamicin ophthalmic ointment.

524.1044d Gentamicin sulfate, betamethasone valerate ointment.

524.1044e Gentamicin sulfate spray.

524.1044f Gentamicin sulfate, betamethasone valerate topical spray.

524.1200 Kanamycin ophthalmic and topical dosage forms.

524.1200a Kanamycin ophthalmic ointment.

524.1200b Kanamycin ophthalmic aqueous solution.

524.1204 Kanamycin sulfate, calcium amphotycin, and hydrocortisone acetate.

524.1240 Levamisole.

Sec.

- 524.1301 Mafenide acetate and nitrofurazone aerosol powder.
- 524.1376 2-Mercaptobenzothiazole solution.
- 524.1443 Miconazole nitrate cream; miconazole nitrate lotion; miconazole nitrate spray.
- 524.1465 Mupirocin ointment.
- 524.1484 Neomycin sulfate ophthalmic and topical dosage forms.
- 524.1484a Neomycin sulfate ophthalmic ointment.
- 524.1484b Neomycin sulfate, 9-fluoroprednisolone acetate, tetracaine hydrochloride, and myristyl-gamma-picolinium chloride, topical powder.
- 524.1484c Neomycin sulfate, isoflupredone acetate, tetracaine hydrochloride ointment.
- 524.1484d Neomycin sulfate, hydrocortisone acetate, tetracaine hydrochloride ear ointment.
- 524.1484e Neomycin sulfate and polymyxin B sulfate ophthalmic solution.
- 524.1484f Neomycin sulfate, prednisolone acetate, tetracaine hydrochloride ear drops.
- 524.1484g Neomycin sulfate-thiabendazole-dexamethasone solution.
- 524.1484h [Reserved]
- 524.1484i Neomycin sulfate, hydrocortisone acetate, sterile ointment.
- 524.1484j [Reserved]
- 524.1484k Neomycin sulfate, prednisolone, tetracaine, and squalane topical-otic suspension.
- 524.1580 Nitrofurazone ophthalmic and topical dosage forms.
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- 524.1580b Nitrofurazone ointment.
- 524.1580c Nitrofurazone soluble powder.
- 524.1580d Nitrofurazone solution.
- 524.1580e Nitrofurazone ointment with butacaine sulfate.
- 524.1600 Nystatin ophthalmic and topical dosage forms.
- 524.1600a Nystatin, neomycin, thiostrepton, and triamcinolone acetonide ointment.
- 524.1600b Nystatin, neomycin, thiostrepton, and triamcinolone acetonide ophthalmic ointment.
- 524.1662 Oxytetracycline hydrochloride ophthalmic and topical dosage forms.
- 524.1662a Oxytetracycline hydrochloride and hydrocortisone spray.
- 524.1662b Oxytetracycline hydrochloride, polymyxin B sulfate ophthalmic ointment.
- 524.1695 Pancreatic dornase.
- 524.1742 N-(Mercaptomethyl) phthalimide S-(O,O-dimethyl phosphorodithioate) emulsifiable liquid.
- 524.1880 Prednisolone-neomycin sulfate ophthalmic ointment.

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- 524.1881 Prednisolone acetate ophthalmic and topical dosage forms.
- 524.1881a [Reserved]
- 524.1881b Prednisolone acetate - neomycin sulfate sterile suspension.
- 524.1883 Prednisolone sodium phosphate-neomycin sulfate ophthalmic ointment.
- 524.1982 Proparacaine hydrochloride ophthalmic solution.
- 524.2080 Ronnel emulsifiable concentrate.
- 524.2101 Selenium disulfide suspension.
- 524.2140 Squalane, pyrethrins and piperonyl butoxide.
- 524.2350 Tolnaftate cream.
- 524.2481 Triamcinolone acetonide cream.
- 524.2620 Liquid crystalline trypsin, Peru balsam, castor oil.
- 524.2640 Tylosin, neomycin eye powder.

AUTHORITY: Sec. 512(i), 82 Stat. 347 (21 U.S.C. 360b(i)); 21 CFR 5.10 and 5.83.

SOURCE: 40 FR 13873, Mar. 27, 1975, unless otherwise noted.

§ 524.86 Amitraz liquid.

(a) *Specifications.* Amitraz liquid contains 19.9 percent amitraz in an organic solvent.

(b) *Sponsor.* See No. 000009 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Indications for use.* For dogs for the treatment of generalized demodicosis (*Demodex canis*).

(2) *Amount.* One 10.6 milliliter bottle per 2 gallons of warm water (250 parts per million) for each treatment, for a total of 3 to 6 treatments, 14 days apart.

(3) *Limitations.* Continue treatment until no viable mites are found in skin scrapings at 2 successive treatments, or until 6 treatments have been applied. Do not use for treatment of localized demodicosis or scabies. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[47 FR 18589, Apr. 30, 1982]

§ 524.321 Cephalonium, polymyxin B sulfate, flumethasone, iodochlorhydroxyquin, piperocaine hydrochloride topical-otic ointment.

(a) *Specifications.* Each gram of the drug contains 10 milligrams cephalonium, 5,000 units polymyxin B sulfate, 0.25 milligram flumethasone, 30 milligrams iodochlorhydroxyquin, and 40 milligrams piperocaine hydrochloride

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in a suitable and harmless ointment base.

(b) *Sponsor.* See No. 000986 in § 510.600(c) of this chapter.

(c) *Conditions of use.* The drug is recommended for dermal and otic use on dogs and cats for the treatment of the following conditions when complicated by bacteria, yeast, or fungus: Pyodermatitis, allergic dermatitis, dermatophytosis, nonspecific pruritus, and external otitis. For mild inflammations a periodic treatment of applying from once daily to twice weekly may be indicated. In severe conditions apply once or twice daily when continuous treatment may be indicated. Dosage per treatment should not exceed 300 milligrams of the ointment. For otic use treatment should not exceed a total of 12 days. For use only by or on the order of a licensed veterinarian.

§ 524.402 Chlorhexidine diacetate ointment.

(a) *Specifications.* The product contains 1 percent of chlorhexidine diacetate in an ointment base.

(b) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used as a topical antiseptic ointment for surface wounds on dogs, cats, and horses.¹

(2) The wound area is carefully cleansed and the drug is applied daily.¹

(3) The drug is not to be used in horses intended for use as food.¹

§ 524.450 Clotrimazole cream.

(a) *Specifications.* Each gram of cream contains 10 milligrams of clotrimazole.

(b) *Sponsor.* See 000859 in § 510.600(c).

(c) *Conditions of use—(1) Amount.* Apply ¼-inch ribbon of cream per square inch of lesion once daily for 2 to 4 weeks.

¹ These conditions are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

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(2) *Indications of use.* For the treatment of fungal infections of dogs and cats caused by *Microsporum canis* and *Trichophyton mentagrophytes*.

(3) *Limitations.* Wash hands thoroughly after use to avoid spread of infection. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 48128, July 18, 1980]

§ 524.463 Copper naphthenate solution.

(a) *Specifications.* The drug contains 37.5 percent copper naphthenate in a suitable solvent.

(b) *Sponsor.* See Nos. 000856 and 017135 in § 510.600(c) of this chapter.

(c) *Conditions of use—Horses and ponies—(1) Amount.* Apply daily to affected hooves until fully healed.

(2) *Indications for use.* As an aid in treating horses and ponies for thrush caused by organisms susceptible to copper naphthenate.

(3) *Limitations.* Use on horses and ponies only. Remove debris and necrotic material before applying. Avoid contact around eyes. Do not use on animals that are raised for food production. Do not contaminate feed. Do not allow runoff of excess drug into hair because contact with the drug may cause some hair loss.

[47 FR 4250, Jan. 29, 1982]

§ 524.520 Cuprimyxin cream.

(a) *Specifications.* The drug contains 0.5 percent cuprimyxin (6-methoxy-1-phenazolin 5, 10-dioxide, cupric complex) in an aqueous cream base.

(b) *Sponsor.* See No. 000004 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) Cuprimyxin is a broad spectrum antibacterial and antifungal cream for the topical treatment of superficial infections in horses, dogs, and cats caused by bacteria, dermatophytes (*Trichophyton* spp., *Microsporum* spp.) and yeast (*Candida albicans*) affecting skin, hair, and external mucosae.

(2) The cream is applied twice daily to affected areas by rubbing into lesions. Treatment should be continued for a few days after clinical recovery to avoid possible relapses.

(3) After application to cutaneous areas, a change in color from dark green to pink is due to the liberation of free myxin from its copper complex.

(4) If no response is seen within seven days, diagnosis and therapy should be reevaluated. If any adverse local reaction is observed after topical application, discontinue treatment.

(5) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13873, Mar. 27, 1975, as amended at 45 FR 56799, Aug. 26, 1980]

§ 524.660 Dimethyl sulfoxide ophthalmic and topical dosage forms.

§ 524.660a Dimethyl sulfoxide solution.

(a) *Specifications.* Dimethyl sulfoxide contains 90 percent of dimethyl sulfoxide and 10 percent of water.

(b) *Sponsor.* See No. 000033 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is used or intended for use as a topical application to reduce acute swelling due to trauma:

(i) In horses administered 2 or 3 times daily in an amount not to exceed 100 milliliters per day. Total duration of therapy should not exceed 30 days.

(ii) In dogs administered 3 or 4 times daily in an amount not to exceed 20 milliliters per day. Total duration of therapy should not exceed 14 days.

(2) Not for use in horses and dogs intended for breeding purposes nor in horses slaughtered for food. Other topical medications should only be used when the dimethyl sulfoxide treated area is thoroughly dry. Do not administer by any other route.

(3) For use by or on the order of a licensed veterinarian.

§ 524.660b Dimethyl sulfoxide gel.

(a) *Specifications.* Dimethyl sulfoxide gel, veterinary contains 90 percent dimethyl sulfoxide in an aqueous gel.

(b) *Sponsor.* See No. 000033 in § 510.600(c) of this chapter.

(c) *Conditions of use.*—(1) *Indications for use.* For use on horses and dogs as a topical application to reduce acute swelling due to trauma.

(2) *Amount.*—(i) *Horses.* Administer 2 or 3 times daily in an amount not to exceed 100 grams per day. Total dura-

tion of therapy should not exceed 30 days.

(ii) *Dogs.* Administer 3 or 4 times daily in an amount not to exceed 20 grams per day. Total duration of therapy should not exceed 14 days.

(3) *Limitations.* Do not use in horses and dogs intended for breeding purposes or in horses slaughtered for food. Restricted to topical use on horses and dogs only. Due to rapid penetrating ability of dimethyl sulfoxide, rubber gloves should be worn when applying the drug. No other medications should be present on the skin prior to application of the drug. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13873, Mar. 27, 1975, as amended at 46 FR 56205, Dec. 20, 1981]

§ 524.900 Famphur.

(a) *Chemical name.* O,O-Dimethyl O-[p-(dimethylsulfamoyl)phenyl] phosphorothioate.

(b) *Specifications.* The drug is in liquid form containing 13.2 percent famphur.

(c) *Sponsor.* See Nos. 010042 and 017800 in § 510.600(c) of this chapter.

(d) *Special considerations.* Do not use on animals simultaneously or within a few days before or after treatment with or exposure to cholinesterase-inhibiting drugs, pesticides, or chemicals.

(e) *Related tolerances.* See 40 CFR 180.233 under the chemical name.

(f) *Conditions of use.* (1) The drug is used as a pour-on formulation for the control of cattle grubs and to reduce cattle lice infestations.

(2) It is used at the rate of 1 ounce per 200 pounds body weight, not to exceed a total dosage of 4 ounces, applied from the shoulder to the tail head as a single treatment. It is applied as soon as possible after heel fly activity ceases. Do not use on lactating dairy cows or dry dairy cows within 21 days of freshening, calves less than 3 months old, animals stressed from castration, over-excitement or dehorning, sick or convalescent animals. Animals may become dehydrated and under stress following shipment. Do not treat until they are in good condition.

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Brahman and Brahman crossbreeds are less tolerant of cholinesterase-inhibiting insecticides than other breeds. Do not treat Brahman bulls.

(3) Do not slaughter within 35 days after treatment. Swine should be eliminated from area where run-off occurs.

[40 FR 13873, Mar. 27, 1975, as amended at 49 FR 34352, Aug. 30, 1984]

§ 524.920 Fenthion.

(a) *Chemical name.* O,O-Dimethyl O-[4-(methylthio)-m-tolyl] phosphorothioate.

(b) *Specifications.* (1) The drug is in a liquid form containing 3 percent of fenthion.

(2) *Sponsor.* See No. 000859 in § 510.600(c) of this chapter.

(3) *Special considerations.* Do not use on animals simultaneously or within a few days before or after treatment with or exposure to cholinesterase-inhibiting drugs, pesticides, or chemicals.

(4) *Related tolerances.* See 40 CFR 180.214.

(5) *Conditions of use.* (i) The drug is used as a pour-on formulation for the control of grubs and lice in beef and nonlactating cattle.

(ii) It is used at the rate of one-half fluid ounce per 100 pounds of body weight placed on the backline of the animal. Only one application per season should be made for grub control and this will also provide initial control of lice. A second application for lice control may be made if animals become reinfested, but no sooner than 35 days after the first treatment. Proper timing of treatment is important for grub control; cattle should be treated as soon as possible after heel-fly activity ceases. Cattle should not be slaughtered within 35 days following a single treatment. If a second application is made for lice control, cattle should not be slaughtered within 45 days of the second treatment. The drug must not be used within 28 days of freshening of dairy cattle. If freshening should occur within 28 days after treatment, do not use milk as human food for the balance of the 28-day interval. Do not treat lactating dairy cattle; calves less than 3 months old; or sick, convales-

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cent, or stressed livestock. Do not treat cattle for 10 days before or after shipping, weaning, or dehorning or after exposure to contagious infectious diseases.

(c) *Specifications.* (1) The drug is in a liquid form containing 20 percent fenthion.

(2) *Sponsor.* See No. 000859 in § 510.600(c) of this chapter.

(3) *Special considerations.* Do not use on animals simultaneously or within a few days before or after treatment with or exposure to cholinesterase-inhibiting drugs, pesticides, or chemicals.

(4) *Related tolerances.* See 40 CFR 180.214.

(5) *Conditions of use.* (i) The drug is used for control of cattle grubs and as an aid in controlling lice on beef cattle and on dairy cattle not of breeding age.

(ii) It is applied as a single application placed on the backline of animals as follows:

Weight of animal	Dosage (milliliters)
150 to 300 lb.....	4
301 to 600 lb.....	8
601 to 900 lb.....	12
901 to 1,200 lb.....	16
Over 1,200 lb.....	20

For most effective results, cattle should be treated as soon as possible after heel-fly activity ceases. Host-parasite reactions such as bloat, salivation, staggering and paralysis may sometimes occur when cattle are treated while the common cattle grub (*Hypoderma lineatum*) is in the gullet, or while the northern cattle grub (*H. bovis*) is in the area of the spinal cord. Cattle should be treated before these stages of grub development. Consult your veterinarian, extension livestock specialist, or extension entomologist regarding the timing of treatment. If it is impossible to determine the area from which the cattle came and/or exact stage of the grubs, it is recommended that the cattle receive only a maintenance ration of low-energy feed during the treatment period. This lessens the likelihood of severe bloat which may occur in cattle on full feed

when the common grub is killed while in the gullet. A second application is required for animals heavily infested with lice or for those which become reinfested. A second application should be made no sooner than 35 days after the first treatment.

(iii) Do not treat dairy cattle of breeding age; calves less than 3 months old; sick, convalescent, or severely stressed livestock.

(iv) Do not treat cattle for 10 days before or after shipping, weaning, de-horning, or after exposure to contagious or infectious diseases.

(v) Do not slaughter within 45 days of treatment.

(d) *Specifications.* (1) The drug is a solution containing either 5.6 or 13.8 percent fenthion. Each concentration is available in 2 volumes which are contained in single-dose applicators.

(2) *Sponsor.* See No. 000859 in § 510.600(c) of this chapter.

(3) *Special considerations.* Fenthion is a cholinesterase inhibitor. Do not use this product on dogs simultaneously with or within 14 days before or after treatment with or exposure to cholinesterase-inhibiting drugs, pesticides, or chemicals. Do not use with flea or tick collars.

(4) *Conditions of use—(i) Amount.* Four to 8 milligrams per kilogram of body weight.

(ii) *Indications for use.* For flea control on dogs only.

(iii) *Limitations.* Apply the contents of the proper size, single-dose tube directly to one spot on the dog's skin. Frequency of repeat treatments depends upon rate of flea reinfestations. Do not use more often than once every 2 weeks. Treatment at 2-week intervals is not to exceed 6 months. Do not use on puppies under 10 weeks of age. Do not use on sick, stressed, or convalescing dogs. Safe use in breeding males has not been established. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13873, Mar. 27, 1975, as amended at 41 FR 16656, Apr. 21, 1976; 42 FR 58741, Nov. 11, 1977; 45 FR 62425, Sept. 19, 1980; 50 FR 19169, May 7, 1985]

§ 524.960 Flumethasone, neomycin sulfate, and polymyxin B sulfate ophthalmic solutions.

(a) *Specifications.* Each milliliter of ophthalmic preparation contains 0.10 milligram flumethasone, 5.0 milligrams neomycin sulfate (3.5 milligrams neomycin base), and 10,000 units of polymyxin B sulfate, with or without hydroxypropyl methylcellulose.

(b) *Sponsor.* See No. 000033 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount—*

(i) *Preparation containing hydroxypropyl methylcellulose.* Dogs: 1 to 2 drops per eye, every 6 hours.

(ii) *Preparation without hydroxypropyl methylcellulose.* Dogs and cats: 2 to 3 drops per eye, every 4 hours.

(2) *Indications for use.* Treatment of the inflammation, edema, and secondary bacterial infections associated with topical ophthalmological conditions of the eye such as corneal injuries, incipient pannus, superficial keratitis, conjunctivitis, acute nongranulomatous anterior uveitis, keratoconjunctivitis, and blepharitis.

(3) *Limitations.* (i) In treating ophthalmological conditions associated with bacterial infections, the drug is contraindicated in those cases in which microorganisms are not susceptible to the antibiotics incorporated in the drug.

(ii) The drug is contraindicated in infectious tuberculous lesions of the eye, early acute stages of viral diseases of the cornea and conjunctiva, herpes simplex lesions of the eye, and fungal infections of the conjunctiva and eyelids.

(iii) The usual precautions and contraindications for corticosteroids and adrenocorticoids are applicable with this drug. Corticosteroids may inhibit essential inflammatory responses intrinsic to the fundamental healing mechanism. Adrenocorticoid compounds have been reported to cause an increase in intraocular pressure. Intraocular pressure should be checked frequently. Ocular reexaminations should be made at frequent intervals during long-term therapy.

§ 524.981a

(iv) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[44 FR 16012, Mar. 16, 1979]

§ 524.981 Fluocinolone acetonide ophthalmic and topical dosage forms.

§ 524.981a Fluocinolone acetonide cream.

(a) *Specifications.* The drug contains 0.025 percent fluocinolone acetonide.

(b) *Sponsor.* See No. 000033 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is indicated for the relief of pruritus and inflammation associated with certain superficial acute and chronic dermatoses in dogs. It is used in the treatment of allergic and acute moist dermatitis and for the relief of superficial inflammation caused by chemical and physical abrasions and burns.

(2) A small amount is applied to the affected area two or three times daily.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

§ 524.981b Fluocinolone acetonide solution.

(a) *Specifications.* The drug contains 0.01 percent fluocinolone acetonide in propylene glycol with citric acid.

(b) *Sponsor.* See No. 000033 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is indicated for the relief of pruritus and inflammation associated with otitis externa and certain superficial acute and chronic dermatoses in the dog. It is also indicated for the relief of pruritus and inflammation associated with acute otitis externa and certain superficial acute and chronic dermatoses in the cat.

(2) A small amount of solution is applied to the affected area 2 or 3 times daily.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

§ 524.981c Fluocinolone acetonide, neomycin sulfate cream.

(a) *Specifications.* The drug contains 0.025 percent fluocinolone acetonide and 0.5 percent neomycin sulfate (0.35 percent neomycin base).

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(b) *Sponsor.* See No. 000033 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used in the relief of pruritus and inflammation associated with superficial acute and chronic dermatoses in dogs. It is used in the treatment of such conditions as allergic and acute moist dermatoses and nonspecific dermatoses in dogs. It is used in the treatment of wound infections in dogs and cats.

(2) A small amount is applied to the infected area two or three times daily.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

§ 524.981d Fluocinolone acetonide, dimethyl sulfoxide solution.

(a) *Specifications.* Each milliliter of solution contains 0.01 percent fluocinolone acetonide and 20 percent dimethyl sulfoxide with propylene glycol and citric acid.

(b) *Sponsor.* See No. 000033 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used in dogs for the relief of impaction commonly present in apparently normal anal sacs, for the reversal of inflammatory changes associated with abnormal anal sacs, and to counteract the offensive odor of anal sac secretions.

(2) It is administered by instillation of 1 to 2 milliliters into each anal sac following expression of anal sac contents. It may be necessary to repeat treatment at 60-day intervals to maintain an odor-free state. The total dosage used should not exceed 2 milliliters per anal sac per treatment.

(3) For use only by or on the order of a licensed veterinarian.

§ 524.981e Fluocinolone acetonide, dimethyl sulfoxide otic solution.

(a) *Specifications.* Each milliliter of solution contains 0.01 percent of fluocinolone acetonide in 60 percent dimethyl sulfoxide with propylene glycol and citric acid.

(b) *Sponsor.* See No. 000033 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used in dogs for the relief of pruritus

inflammation associated with acute and chronic otitis.

(2) It is administered at 4 to 6 drops (2 milliliter) twice daily into the ear canal for a maximum period of 14 days. The total dosage used should not exceed 17 milliliters. The ear canal should be cleansed by some appropriate method prior to instillation of the solution and the ear should be massaged gently following instillation.

(3) There should be careful initial evaluation and followup of infected animals. Incomplete response or exacerbation of corticosteroid-responsive lesions may be due to the presence of an infection which requires identification, antibiotic sensitivity testing, and use of the appropriate antimicrobial agent. As with any corticosteroid, animals with a generalized infection should not be treated with this product without proper supportive antimicrobial therapy. Preparations with dimethyl sulfoxide should not be used in pregnant animals. For use by or on the order of a licensed veterinarian.

4.1005 Furazolidone aerosol powder.

(a) *Specifications.* The product consists either 4 or 10 percent furazolidone in inert dispersing agent and propellant.

(b) *Sponsors.* (1) See No. 000007 in § 510.600(c) of this chapter for use of 10 percent product as in paragraphs (c)(2) (i) through (iii) of this section.

(2) See No. 017135 for use of the 4 percent product as in paragraph (c)(iv) of this section.

(c) *Conditions of use—(1) Amount.* Hold container about 6 to 12 inches from the eye or affected area and spray only enough powder to impart a light yellow color.

(2) *Indications of use—(i) Dogs.* For treatment or prevention of bacterial infection of superficial wounds, abrasions, lacerations, and pyogenic dermatitis.

(ii) *Horses.* For treatment or prevention of bacterial infection of superficial wounds, abrasions, lacerations, following firing (heat or electrocautery).

(iii) *Cattle.* For treatment of bacterial infections of the bovine eye and treatment and to reduce the incidence

of additional cases of infectious bovine keratoconjunctivitis (pink eye) caused by *Moraxella bovis*.

(iv) *Horses and ponies.* For treatment or prevention of bacterial infection of superficial wounds, abrasions, and lacerations caused by *Staphylococcus aureus*, *Streptococcus spp.* and *Proteus spp.* sensitive to furazolidone.

(3) *Limitations.* For topical application in horses, ponies, and dogs: Clean affected area thoroughly, apply drug once or twice daily, and repeat treatment as required. For treatment of bacterial infections of the bovine eye and infectious bovine keratoconjunctivitis (pink eye) caused by *Moraxella bovis*: Treat affected eyes once daily on each of 3 to 5 consecutive days; to reduce incidence of additional cases of infectious keratoconjunctivitis also medicate unaffected eyes. Evidence of clinical improvement of bovine eye infections should be noticeable after 5 treatments; if not, reconsult veterinarian. Use only as recommended by a veterinarian in treatment of puncture wounds, wounds requiring surgical debridement or suturing, those of a chronic nature involving proud flesh, generalized and chronic infections of the skin, and those skin conditions associated with intense itching. If redness, irritation, or swelling persists or increases, discontinue use and reconsult veterinarian. Not for use in horses intended for food.

[45 FR 49543, July 25, 1980, as amended at 50 FR 30153, July 24, 1985]

§ 524.1044 Gentamicin sulfate ophthalmic and topical dosage forms.

[41 FR 14189, Apr. 2, 1976]

§ 524.1044a Gentamicin ophthalmic solution.

(a) *Specifications.* Each milliliter of sterile aqueous solution contains gentamicin sulfate equivalent to 3 milligrams of gentamicin.

(b) *Sponsor.* See No. 000061 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used in dogs and cats for the topical treatment of infections of the conjunctiva caused by susceptible bacteria.

(2) Administer 1 or 2 drops into the conjunctival sac 2 to 4 times a day.

§ 524.1044b

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[41 FR 14189, Apr. 2, 1976, as amended at 52 FR 7832, Mar. 13, 1987]

§ 524.1044b Gentamicin sulfate, betamethasone valerate otic solution.

(a) *Specifications.* Each cubic centimeter of solution contains gentamicin sulfate equivalent to 3 milligrams of gentamicin base and betamethasone valerate equivalent to 1 milligram of betamethasone alcohol.

(b) *Sponsor.* See No. 000061 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used or indicated for use in dogs in the treatment of acute and chronic otitis externa caused by bacteria sensitive to gentamicin; the drug is also used or indicated for use in dogs and cats in the treatment of superficial infected lesions caused by bacteria sensitive to gentamicin.

(2)(i) For the treatment of acute and chronic canine otitis externa caused by bacteria sensitive to gentamicin, the drug is administered by instillation of 3 to 8 drops of solution into the ear canal twice daily for 7 to 14 days. Duration of treatment will depend upon the severity of the condition and the response obtained. The duration of treatment and/or frequency of the dosage may be reduced but care should be taken not to discontinue therapy prematurely. The external ear and ear canal should be properly cleaned and dried before treatment. Remove foreign material, debris, crusted exudates, etc., with suitable nonirritating solutions. Excessive hair should be clipped from the treatment area of the external ear.

(ii) For the treatment of canine and feline superficial infected lesions caused by bacteria sensitive to gentamicin, the lesion and adjacent area should be properly cleaned before treatment. Excessive hair should be removed. A sufficient amount of the drug should be applied to cover the treatment area. The drug should be administered twice daily for 7 to 14 days.

(3) If hypersensitivity to any of the components occurs treatment with this product should be discontinued

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and appropriate therapy instituted. Concomitant use with other drugs known to induce ototoxicity is not recommended. This preparation should not be used in conditions where corticosteroids are contraindicated. Do not administer parenteral corticosteroids during treatment with this drug. The antibiotic sensitivity of the pathogenic organism should be determined prior to use of this preparation.

(4) For use by or on the order of a licensed veterinarian.

[40 FR 13873, Mar. 27, 1975. Redesignated at 41 FR 14189, Apr. 2, 1976, and amended at 52 FR 7832, Mar. 13, 1987]

§ 524.1044c Gentamicin ophthalmic ointment.

(a) *Specifications.* Each gram of sterile ointment contains gentamicin sulfate equivalent to 3 milligrams of gentamicin.

(b) *Sponsor.* See No. 000061 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used on dogs and cats for topical treatment of conjunctivitis caused by susceptible bacteria.

(2) Apply approximately a ½-inch strip to the affected eye 2 to 4 times a day.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[41 FR 14188, Apr. 2, 1976, as amended at 52 FR 7832, Mar. 13, 1987]

§ 524.1044d Gentamicin sulfate, betamethasone valerate ointment.

(a) *Specifications.* Each gram of ointment contains gentamicin sulfate equivalent to 3 milligrams of gentamicin base and betamethasone valerate equivalent to 1 milligram of betamethasone.

(b) *Sponsor.* See No. 000061 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used or indicated for use in dogs in the treatment of acute and chronic canine otitis externa and canine infected superficial lesions caused by bacteria sensitive to gentamicin.

(2)(i) For the treatment of acute and chronic canine otitis externa the drug is administered by instillation of 3 to 8 drops into the ear canal twice daily for

7 days. The external ear and ear canal should be properly cleaned and dried before treatment. Remove foreign material, debris, crusted exudates, etc., with suitable nonirritating solutions. Excessive hair should be clipped from the treatment area of the external ear.

(ii) For the treatment of canine infected superficial lesions, the lesion and adjacent area should be properly cleaned before treatment. Excessive hair should be removed. A sufficient amount of the drug should be applied to cover the treatment area. The drug should be administered twice daily for 7 to 14 days.

(3) If hypersensitivity to any of the components occurs, treatment should be discontinued and appropriate therapy instituted. Concomitant use of drugs known to induce ototoxicity should be avoided. Observe patients for signs of adrenocortical overdosage. The antibiotic susceptibility of the pathogenic organism should be determined prior to use of this preparation. Administration of recommended doses beyond 7 days may result in delayed wound healing. Animals treated longer than 7 days should be monitored closely.

(4) For use by or on the order of a licensed veterinarian.

[47 FR 26378, June 18, 1982, as amended at 52 FR 7832, Mar. 13, 1987]

§ 524.1044e Gentamicin sulfate spray.

(a) *Specification.* Each milliliter of sterile aqueous solution contains gentamicin sulfate equivalent to 1.07 milligrams of gentamicin.

(b) *Sponsor.* See No. 000061 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is indicated for the treatment of pink eye in cattle (infectious bovine keratoconjunctivitis) caused by *Moraxella bovis*.

(2) One actuation of the sprayer delivers 0.7 milliliter containing 0.75 milligram gentamicin. The sprayer should be held upright 3 to 6 inches from the affected eye, with the opening directed towards the eye, and pumped once. It is advisable to treat once a day for up to 3 days.

(3) Conditions other than bacterial infections of the bovine eye and infectious keratoconjunctivitis caused by

Moraxella bovis may produce similar signs. If conditions persists or increases, discontinue use and consult veterinarian.

[48 FR 41157, Sept. 14, 1983, as amended 52 FR 7833, Mar. 13, 1987]

§ 524.1044f Gentamicin sulfate, betamethasone valerate topical spray.

(a) *Specifications.* Each milliliter of spray contains gentamicin sulfate equivalent to 0.57 milligram of gentamicin base and betamethasone valerate equivalent to 0.284 milligram of betamethasone.

(b) *Sponsor.* See No. 000061 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used in dogs in the treatment of infected superficial lesions caused by bacteria sensitive to gentamicin.

(2) For the treatment of infected superficial lesions, the lesion and adjacent area should be properly cleaned before treatment. Excessive hair should be removed. Hold bottle upright 3 to 6 inches from the lesion and depress the sprayer head twice. One actuation of the sprayer delivers 0.7 milliliter of the spray. The drug should be administered with two spray actuations 2 to 4 times daily for 7 days.

(3) If hypersensitivity to any of the components occurs, treatment should be discontinued and appropriate therapy instituted. The antibiotic susceptibility of the pathogenic organism should be determined prior to use of this preparation. Administration of recommended doses beyond 7 days may result in delayed wound healing. Animals treated longer than 7 days should be monitored closely.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[50 FR 740, Jan. 7, 1985, as amended at 52 FR 7833, Mar. 13, 1987]

§ 524.1200 Kanamycin ophthalmic and topical dosage forms.

§ 524.1200a Kanamycin ophthalmic ointment.

(a) *Specifications.* (1) The kanamycin used conforms to the standards of

§ 524.1200b

identity, strength, quality, and purity prescribed by § 444.30 of this chapter.

(2) The drug, which is in a suitable and harmless ointment base, contains 3.5 milligrams of kanamycin activity (as the sulfate) per gram of ointment.

(b) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(c) *Conditions of use.* It is indicated for use in dogs in various eye infections due to kanamycin sensitive bacteria. It is used treating conditions such as conjunctivitis, blepharitis, dacryocystitis, keratitis, and corneal ulcerations and as a prophylactic in traumatic conditions, removal of foreign bodies, and intraocular surgery. Apply a thin film to the affected eye three or four times daily or more frequently if deemed advisable. Treatment should be continued for at least 48 hours after the eye appears normal. For use only by or on the order of a licensed veterinarian.

[40 FR 13858, Mar. 27, 1975, as amended at 53 FR 27851, July 25, 1988]

§ 524.1200b Kanamycin ophthalmic aqueous solution.

(a) *Specifications.* (1) The kanamycin used conforms to the standards of identity, strength, quality, and purity prescribed by § 444.30 of this chapter.

(2) The drug, which is in an aqueous solution including suitable and harmless preservatives and buffer substances, contains 10.0 milligrams of kanamycin activity (as the sulfate) per cubic centimeter of solution.

(b) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(c) *Conditions of use.* It is indicated for use in dogs in various eye infections due to kanamycin sensitive bacteria. It is used in treating conditions such as conjunctivitis, blepharitis, dacryocystitis, keratitis, and corneal ulcerations and as a prophylactic in traumatic conditions, removal of foreign bodies, and intraocular surgery. Instill a few drops into the affected eye every 3 hours or more frequently if deemed advisable. Administer as frequently as possible for the first 48 hours, after which the frequency of applications may be decreased. Treatment should be continued for at least 48 hours after the eye appears normal.

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For use only by or on the order of a licensed veterinarian.

[40 FR 13858, Mar. 27, 1975, as amended at 53 FR 27851, July 25, 1988]

§ 524.1204 Kanamycin sulfate, calcium amphomycin, and hydrocortisone acetate.

(a) *Specifications.* (1) The kanamycin used conforms to the standards of identity, strength, quality, and purity prescribed by § 444.30(a)(1) of this chapter.

(2) Calcium amphomycin is the calcium salt of amphomycin. It conforms to the following specifications:

(i) Its potency is not less than 963 micrograms of amphomycin per milligram;

(ii) Its moisture content is not more than 10 percent; and

(iii) Its pH in a 2-percent aqueous suspension is 6.0 to 7.5.

(3) The drug is in a water-miscible ointment or cream base and each gram of ointment or cream contains: 5.0 milligrams of kanamycin activity as the sulfate, 5.0 milligrams of amphomycin activity as the calcium salt, and 10.0 milligrams of hydrocortisone acetate.

(b) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is indicated for use in dogs in the following conditions associated with bacterial infections caused by organisms susceptible to one or both antibiotics: Acute otitis externa, furunculosis, folliculitis, pruritus, anal gland infections, erythema, decubital ulcer, superficial wounds, and superficial abscesses.

(2) The ointment should be applied to the affected areas of the skin at least twice daily. In severe or widespread lesions it may be desirable to apply the ointment more than twice daily. After some improvement is observed, treatment can usually be reduced to once daily. Before application, hair in the affected area should be closely clipped and the area should be thoroughly cleansed of crusts, scales, dirt, or other detritus. When treating infections of the anal gland, the drug should be introduced into the orifice of the gland and not through any fistulous tract. If no response is

erident in 7 days, diagnosis and therapy should be reevaluated.

(3) For use only by or on the order of a licensed veterinarian.

[40 FR 13858, Mar. 27, 1975, as amended at 53 FR 12512, Apr. 15, 1988; 53 FR 27851, July 25, 1988]

§ 524.1240 Levamisole.

(a) *Specifications.* The drug contains 200 milligrams of levamisole per milliliter of diethylene glycol monobutyl ether (DGME) solution.

(b) *Sponsor.* See 010042 and 011716 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See § 556.350 of this chapter.

(d) *Conditions of use. Cattle*—(1) *Amount.* 2.5 milliliters per 110 pounds (10 milligrams of levamisole per kilogram) of body weight as a single dose topically to the back of the animal.

(2) *Indications for use.* Anthelmintic effective against stomach worms (*Haemonchus*, *Trichostrongylus*, *Ostertaria*), intestinal worms (*Trichostrongylus*, *Cooperia*, *Nematodirus*, *Bunostomum*, *Oesophagostomum*, *Chabertia*), and lungworms (*Dictyocaulus*).

(3) *Limitations.* Conditions of constant helminth exposure may require retreatment within 2 to 4 weeks after the first treatment. Cattle must not be slaughtered within 9 days following last treatment. Do not administer to dairy animals of breeding age. Do not treat animals before dipping or prior to exposure to heavy rain. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism, and before using in severely debilitated animals.

[52 FR 10887, Apr. 6, 1987, as amended at 53 FR 7604, Mar. 9, 1988]

§ 524.1301 Mafenide acetate and nitrofurazone aerosol powder.

(a) *Specifications.* The product is in an aerosol preparation which contains .61 percent of mafenide acetate and .12 percent of nitrofurazone as active ingredients.

(b) *Approvals.* To No. 000934 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is intended for topical application to dogs for the prophylactic and therapeutic treatment of wound infections and pyogenic dermatitis caused by a variety

of gram-positive and gram-negative bacteria including *Staphylococcus* sp., *Streptococcus* sp., *Proteus* sp., *Pseudomonas* sp., *Escherichia coli* and *Aerobacter aerogenes*, and virulent strains of *Pseudomonas aeruginosa*.

(2) After cleansing the area to be treated, apply a light coat of the drug. Use once or twice daily, usually for up to 5 days.

(3) Avoid application to eyes.

(4) Occasional transitory local reactions (irritation) may occur.

(5) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13873, Mar. 27, 1975, as amended at 42 FR 36995, July 19, 1977]

§ 524.1376 2-Mercaptobenzothiazole solution.

(a) *Specifications.* The drug contains 1.3 percent 2-mercaptobenzothiazole in a suitable solvent.

(b) *Sponsor.* See 011509 in § 510.600(c) of this chapter.

(c) *Conditions of use*—(1) *Amount.* Apply twice daily to affected area.

(2) *Indications for use.* For dogs as an aid in treating moist dermatitis and hotspots and as first aid for scrapes and abrasions.

(3) *Limitations.* Clip hair from affected area before applying. If no improvement is seen within 1 week, consult a veterinarian.

[48 FR 15618, Apr. 12, 1983]

§ 524.1443 Miconazole nitrate cream; miconazole nitrate lotion; miconazole nitrate spray.

(a) *Specifications.* (1) The cream contains 23 milligrams of miconazole nitrate (equivalent to 20 milligrams of miconazole base) per gram.

(2) The lotion contains 1.15 percent of miconazole nitrate (equivalent to 1 percent miconazole base).

(3) The spray product consists of a dispensing container, sprayer pump assembly, and lotion which contains 1.15 percent of miconazole nitrate (equivalent to 1-percent miconazole base).

(b) *Sponsor.* See No. 011716 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) Miconazole nitrate is an antifungal agent for topical treatment of infections in dogs and

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cats caused by *Microsporum canis*, *Microsporum gypseum*, and *Trichophyton mentagrophytes*.

(2) Apply once daily by rubbing into or spraying a light covering on the infected site and the immediate surrounding vicinity. Continue treatment for 2 to 4 weeks until infection is completely eradicated as determined by appropriate laboratory examination.

(3) Accurate diagnosis of infecting organism is essential. Identify by microscopic examination of a mounting of infected tissue in potassium hydroxide solution or by culture on an appropriate medium.

(4) If no improvement is observed in 2 weeks, reevaluate diagnosis and therapy.

(5) Avoid contact with eyes since irritation may result.

(6) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13873, Mar. 27, 1975, as amended at 53 FR 26242, July 12, 1988]

§ 524.1465 Mupirocin ointment.

(a) *Specifications*. Each gram contains 20 milligrams of mupirocin.

(b) *Sponsor*. See No. 000029 in § 510.600(c) of this chapter.

(c) *Conditions of use*—(1) *Dogs*:

(i) *Indications for use*. Topical treatment of bacterial infections of the skin, including superficial pyoderma, caused by susceptible strains of *Staphylococcus aureus* and *Staphylococcus intermedius*.

(ii) *Limitations*. Apply twice daily. Treatment should not exceed 30 days. Because of potential hazard of nephrotoxicity due to polyethylene glycol content, care should be exercised in treating deep lesions. Safety of use in pregnant or breeding animals has not been determined. Not for ophthalmic use. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(2) [Reserved]

[53 FR 39085, Oct. 5, 1988]

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§ 524.1484 Neomycin sulfate ophthalmic and topical dosage forms.

§ 524.1484a Neomycin sulfate ophthalmic ointment.

(a) *Specifications*. Each gram of the ointment contains 5 milligrams of neomycin sulfate equivalent in activity to 3.5 milligrams of neomycin base.

(b) *Sponsor*. See No. 017030 in § 510.600(c) of this chapter.

(c) *Conditions of use*. (1) The drug is intended for use in dogs and cats for the treatment of superficial ocular bacterial infections limited to the conjunctival or the anterior segment of the eye.

(2) The drug is applied four times each day.

(3) The drug is applied by inserting the tip of the tube beneath the lower lid and by expressing a small quantity of ointment into the conjunctival sac. The tip of the tube should not come in contact with the eye surface.

(4) Severe infections should be supplemented by systemic therapy.

(5) Prolonged administration of the drug may permit overgrowth of organisms that are not susceptible to neomycin. If new infections due to bacteria or fungi appear during therapy, appropriate measures should be taken.

(6) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13873, Mar. 27, 1975, as amended at 44 FR 49866, Aug. 24, 1979]

§ 524.1484b Neomycin sulfate, isoflupredone acetate, tetracaine hydrochloride, and myristyl-gammapiocolinium chloride, topical powder.

(a) *Specifications*. The product contains 5 milligrams of neomycin sulfate, equivalent to 3.5 milligrams of neomycin base, 1 milligram of isoflupredone acetate, 5 milligrams of tetracaine hydrochloride and .2 milligram of myristyl-gamma-picolinium chloride in each gram of the product in a special adherent powder base.

(b) *Sponsor*. See No. 000009 in § 510.600(c) of this chapter.

(c) *Conditions of use*. (1) It is used in horses, dogs, and cats in the treatment or adjunctive therapy of certain ear and skin conditions when such condi-

tions are caused by or associated with neomycin-susceptible organisms and/or allergy. In addition the product is indicated as superficial dressing applied to minor cuts, wounds, lacerations, abrasions, and for postsurgical application where reduction of pain and inflammatory response is deemed desirable. The product may be used as a dusting powder following amputation of tails, claws, and dew-claws and following ear trimming, castrating, and such surgical procedures as ovari-hysterectomies. The product may also be used in the treatment of acute otitis externa in dogs, acute moist dermatitis and interdigital dermatitis in dogs.

(2) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13873, Mar. 27, 1975, as amended at 43 FR 18172, Apr. 28, 1978]

§ 524.1484c Neomycin sulfate, isoflupredone acetate, tetracaine hydrochloride ointment.

(a) *Specifications.* The drug contains 5 milligrams of neomycin sulfate (equivalent to 3.5 milligrams of neomycin base), 1 milligram of isoflupredone acetate, and 5 milligrams of tetracaine hydrochloride in each gram of ointment.

(b) *Sponsor.* See No. 000009 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is used in treating such conditions as acute otitis externa in dogs and to a lesser degree, chronic otitis externa in dogs. It also is effective in treating anal gland infections and moist dermatitis in the dog and is a useful dressing for minor cuts, lacerations, abrasions, and post-surgical therapy in the horse, cat, and dog. It may also be used following amputation of dewclaws, tails and claws, following ear trimming and castrating operations.

(2) In treatment of otitis externa and other inflammatory conditions of the external ear canal, a quantity of ointment sufficient to fill the external ear canal may be applied one to three times daily. When used on the skin or mucous membranes, the affected area should be cleansed, and a small amount of the ointment applied and spread or rubbed in gently. The in-

volved area may be treated one to three times a day and these daily applications continued in accordance with the clinical response.

(3) Tetracaine and neomycin have the potential to sensitize. Care should be taken to observe animals being treated for evidence of hypersensitivity or allergy to the drug. If such signs are noted, therapy with the drug should be stopped. Treatment should be limited to the period when local anesthesia is essential to control self-inflicted trauma.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13873, Mar. 27, 1975, as amended at 43 FR 18172, Apr. 28, 1978]

§ 524.1484d Neomycin sulfate, hydrocortisone acetate, tetracaine hydrochloride ear ointment.

(a) *Specifications.* The product contains 5 milligrams of neomycin sulfate, equivalent to 3.5 milligrams of neomycin base, 5 milligrams of hydrocortisone acetate, and 5 milligrams of tetracaine hydrochloride in each gram of ointment.

(b) *Sponsor.* See No. 000009 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is indicated for treating acute otitis externa and, to a lesser degree, chronic otitis externa in dogs and cats. In treatment of ear canker and other inflammatory conditions of the external ear canal, a quantity of ointment sufficient to fill the external ear canal may be applied one to three times daily.¹

(2) Tetracaine and neomycin have the potential to sensitize. Care should be taken to observe animals being treated for evidence of hypersensitivity or allergy to the product. If such signs are noted, therapy with the product should be stopped. Incomplete response or exacerbation of corticosteroid responsive lesions may be due to the presence of nonsusceptible organisms or to prolonged use of antibiotic-containing preparations resulting in overgrowth of nonsusceptible organisms, particularly *Monilia*.¹

¹ These conditions are NAS/NRC reviewed and deemed effective. Applications
Continued

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(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

[40 FR 13873, Mar. 27, 1975, as amended at 49 FR 21922, May 24, 1984]

§ 524.1484e Neomycin sulfate and polymyxin B sulfate ophthalmic solution.

(a) *Specifications.* Each milliliter of the ophthalmic preparation contains 5.0 milligrams neomycin sulfate (3.5 milligrams neomycin base), and 10,000 Units of polymyxin B sulfate.

(b) *Sponsor.* See No. 000033 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is recommended for the treatment of bacterial infections associated with topical ophthalmological conditions such as corneal injuries, superficial keratitis, conjunctivitis, keratoconjunctivitis, and blepharitis in the dog.

(2) The recommended dosage is 1 to 2 drops per eye every 6 hours.

(3) In treating ophthalmological conditions associated with bacterial infections the drug is contraindicated in those cases in which microorganisms are nonsusceptible to the antibiotics incorporated in the drug.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

§ 524.1484f Neomycin sulfate, prednisolone acetate, tetracaine hydrochloride eardrops.

(a) *Specifications.* The product contains 5 milligrams of neomycin sulfate equivalent to 3.5 milligrams of neomycin base, 2.5 milligrams of prednisolone acetate, and 5 milligrams of tetracaine hydrochloride in each milliliter of sterile suspension.

(b) *Sponsor.* See No. 000009 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is useful in treating such conditions as acute otitis externa and, to a lesser degree, chronic otitis externa in dogs and cats. It is indicated as treatment or adjunctive therapy of certain ear conditions in dogs and cats caused by or associated with neomycin-susceptible orga-

for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

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nisms and/or allergy. In otitis externa, 2 to 6 drops may be placed in the external ear canal two or three times daily.¹

(2) Incomplete response or exacerbation of corticosteroid responsive lesions may be due to the presence of nonsusceptible organisms or to prolonged use of antibiotic-containing preparations resulting in overgrowth of nonsusceptible organisms, particularly *Monilia*. Thus, if improvement is not noted within 2 or 3 days, or if redness, irritation, or swelling persists or increases, the diagnosis should be re-determined and appropriate therapeutic measures initiated. Tetracaine and neomycin have the potential to sensitize. Care should be taken to observe animals being treated for evidence of hypersensitivity or allergy. If such signs are noted, therapy should be stopped.¹

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

§ 524.1484g Neomycin sulfate-thiabendazole-dexamethasone solution.

(a) *Specifications.* Each cubic centimeter of neomycin sulfate-thiabendazole-dexamethasone solution contains 40 milligrams of thiabendazole, 3.2 milligrams of neomycin (from neomycin sulfate), and 1 milligram of dexamethasone.

(b) *Sponsor.* See No. 000006 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is recommended for use as an aid in the treatment of bacterial, mycotic, and inflammatory dermatoses and otitis externa in dogs and cats.

(2) In treating dermatoses affecting areas other than the ear, the surface of the lesions should be well moistened (two to four drops per square inch) twice daily. In treating otitis externa, five to 15 drops of the drug should be instilled in the ear twice daily. The drug is limited to 7 days maximum duration of administration.

¹ These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(3) For use only by or on order of a licensed veterinarian.

§ 524.1484h [Reserved]

§ 524.1484i Neomycin sulfate, hydrocortisone acetate, sterile ointment.

(a) *Specifications.* The drug contains milligrams of neomycin sulfate, equivalent to 3.5 milligrams of neomycin base, and 5 milligrams of hydrocortisone acetate in each gram of ointment.¹

(b) *Sponsor.* No. 000009 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) *Amount.* Apply three or four times daily into the conjunctival sac. With improvement, frequency may be reduced to two or three times daily. For treatment of ear canker and other inflammatory conditions of the external ear canal, fill external ear canal one to three times daily.¹

(2) *Indications for use.* For treating infections, allergic, and traumatic keratitis, conjunctivitis, acute otitis externa and, to a lesser degree, chronic otitis externa in dogs and cats.¹

(3) *Limitations.* All topical ophthalmic preparations containing corticosteroids, with or without an antimicrobial agent, are contraindicated in the initial treatment of corneal ulcers. They should not be used until infection is under control and corneal regeneration is well underway. Incomplete response or exacerbation of corticosteroid responsive lesions may be due to the presence of nonsusceptible organisms or to prolonged use on antibiotic-containing preparations resulting in overgrowth of nonsusceptible organisms, particularly *Monilia*. Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

FR 40456, Sept. 12, 1978]

These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

§ 524.1484j [Reserved]

§ 524.1484k Neomycin sulfate, prednisolone, tetracaine, and squalane topical otic suspension.

(a) *Specifications.* Each milliliter of suspension contains 5 milligrams neomycin sulfate (equivalent to 3.5 milligrams neomycin base), 2 milligrams prednisolone, 5 milligrams tetracaine, and 0.25 milliliter squalane.

(b) *Sponsor.* See 017030 in § 510.600(c) of this chapter.

(c) *Conditions of use.*—(1) *Amount.* 2 to 3 applications daily or as needed.

(2) *Indications for use.* Indicated for use in dogs and cats for treating acute otitis externa and as adjunctive therapy in management of chronic otitis externa. The product may also be used for treating moist dermatitis in dogs.

(3) *Limitations.* Tetracaine and neomycin have the potential to sensitize. If signs of irritation or sensitivity develop, discontinue use. Prolonged use of this product may result in overgrowth of nonsusceptible organisms. If new infections due to bacteria or fungi appear during therapy, appropriate measures should be taken. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[48 FR 5265, Feb. 4, 1983; 48 FR 8055, Feb. 25, 1983]

§ 524.1580 Nitrofurazone ophthalmic and topical dosage forms.

§ 524.1580a Nitrofurazone - nifuroxime - dipiperdon hydrochloride ear solution.

(a) *Specifications.* Nitrofurazone-nifuroxime-dipiperdon hydrochloride ear solution contains on a weight-in-weight basis 0.2 percent nitrofurazone; 0.375 percent nifuroxime, and 2 percent dipiperdon hydrochloride in a water soluble vehicle.

(b) *Sponsor.* See No. 000149 in § 510.600(c) of this chapter.

(c) *Conditions of use.* The drug is recommended for use in dogs in the treatment of bacterial ear infections caused by organisms sensitive to nitrofurazone and/or nifuroxime. It is administered two or three times daily. The drug is not intended for prolonged use. Sensitivity to the drug may develop. If redness, irritation, or

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swelling persists or increases, use of the drug should be discontinued and a veterinarian consulted.¹

[40 FR 13873, Mar. 27, 1975. Redesignated at 45 FR 43402, June 27, 1980, and amended at 46 FR 1261, Jan. 6, 1981]

§ 524.1580b Nitrofurazone ointment.

(a) *Specifications.* The drug contains 0.2 percent nitrofurazone in a water-soluble base.

(b) *Sponsor.* For use in dogs, cats, and horses see Nos. 000857, 000864, 011519, 015579, 023851, 053617, and 054273 in § 510.600(c) of this chapter. For use in dogs and horses see No. 017135 in § 510.600(c) of this chapter. For use in horses see No. 017153 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Indications for use.* For prevention or treatment of surface bacterial infections of wounds, burns, and cutaneous ulcers of dogs, cats, or horses.¹

(2) *Limitations.* Apply directly on the lesion with a spatula or first place on a piece of gauze. Use of a bandage is optional. The preparation should remain on the lesion for at least 24 hours. The dressing may be changed several times daily or left on the lesion for a longer period. For use only on dogs, cats, and horses (not for food use). In case of deep or puncture wounds or serious burns, use only as recommended by veterinarian. If redness, irritation, or swelling persists or increases, discontinue use; consult veterinarian.¹

[46 FR 43402, June 27, 1980, as amended at 49 FR 6476, Feb. 22, 1984; 50 FR 49373, Dec. 2, 1985; 52 FR 18691, May 19, 1987; 53 FR 32610, Aug. 26, 1988; 53 FR 40728, Oct. 18, 1988]

§ 524.1580c Nitrofurazone soluble powder.

(a) *Specifications.* The drug contains 0.2 percent nitrofurazone in a water-soluble base.

(b) *Sponsor.* See Nos. 011519 and 054273 in § 510.600(c) of this chapter.

¹These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

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(c) *Conditions of use—(1) Amount.* Apply several times daily to the lesion or affected area from the plastic squeeze bottle.

(2) *Indications for use.* For prevention or treatment of surface bacterial infections of wounds, burns, skin ulcers, and abscesses after incision.¹

(3) *Limitations.* In case of deep or puncture wounds or serious burns, use only as recommended by veterinarian. If redness, irritation, or swelling persists or increases, discontinue use; consult veterinarian. For use only on dogs, cats, and horses (not for food use).¹

[45 FR 43402, June 27, 1980, as amended at 47 FR 43368, Oct. 1, 1982; 48 FR 28984, June 24, 1983; 53 FR 40728, Oct. 18, 1988]

§ 524.1580d Nitrofurazone solution.

(a) *Specifications.* The drug is an aqueous solution containing 0.2 percent nitrofurazone.

(b) *Sponsors.* See 000857, 051259, 053617, and 054273 in § 510.600(c) of this chapter for use as in paragraphs (d) (1) and (2) of this section. See 017153 in § 510.600(c) of this chapter for use in paragraph (d)(1) of this section.

(c) *NAS/NRC status.* These conditions are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(d) *Conditions of use—(1) Dogs, cats, and horses—(i) Indications for use.* For prevention or treatment of topical bacterial infections.

(ii) *Amount.* Apply directly to affected areas, or dilute and apply as a wet dressing.

(iii) *Limitations.* For surface bacterial infections apply directly to lesions. For wet dressing, dilute with two or three parts sterile water or saline and apply several times daily or beneath dressing for several days. In case of deep or puncture wounds or serious burns, consult a veterinarian. If redness, irritation, or swelling increases or persists, discontinue use and consult a veterinarian. Not for use for horses intended for food.

(2) *Horses*—(i) *Indications for use.* For equine genital tract infections and for impaired fertility due to strains of *Salmonella*, *Staphylococcus*, *Streptococcus*, *Pseudomonas*, *Escherichia coli*, and *Vibrio fetus* sensitive to nitrofurazone.

(ii) *Amount.* For female equine genital tract infections, instill aseptically 30 to 90 milliliters into affected areas once daily. For impaired fertility instill 30 milliliters into the uterus 4 to 48 hours after breeding.

(iii) *Limitations.* For treatment of genital tract infections, repeat treatment until 48 hours after remission of clinical symptoms or bacterial cultures show recovery. Do not use in horses intended for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[47 FR 8347, Feb. 26, 1982, as amended at 52 FR 4897, Feb. 18, 1987; 52 FR 18691, May 10, 1987; 52 FR 36023, Sept. 25, 1987; 53 FR 32610, Aug. 26, 1988; 53 FR 40728, Oct. 18, 1988]

§ 524.1580e Nitrofurazone ointment with butacaine sulfate.

(a) *Specifications.* The drug contains 0.2 percent nitrofurazone and 0.5 percent butacaine sulfate in a water-soluble base.

(b) *Sponsor.* See No. 051259 in § 510.600(c) of this chapter.

(c) *Conditions of use*—(1) *Indications for use.* For prevention or treatment of surface bacterial infections of ears, wounds, burns, and cutaneous ulcers of dogs, cats, and horses.¹

(2) *Limitations.* Apply directly on the lesion with a spatula or first place on a piece of gauze. Use of a bandage is optional. The preparation should remain on the lesion for at least 24 hours. The dressing may be changed several times daily or left on the lesion for a longer period. For use only on dogs, cats, and horses (not for food use). In case of deep or puncture wounds or serious burns, use only as recommended by a veterinarian. If

redness, irritation, or swelling persists or increases, discontinue use; consult veterinarian.¹

[49 FR 9417, Mar. 13, 1984]

§ 524.1600 Nystatin ophthalmic and topical dosage forms.

§ 524.1600a Nystatin, neomycin, thiostrepton, and triamcinolone acetonide ointment.

(a) *Specifications.* Each milliliter of petrolatum base or each gram of vanishing cream base ointment contains: 100,000 units of nystatin; neomycin sulfate equivalent to 2.5 milligrams of neomycin base; 2,500 units of thiostrepton; and 1.0 milligram of triamcinolone acetonide.

(b) *Sponsor.* See Nos. 025463, 051259, and 053501 in § 510.600(c) of this chapter.

(c) *Conditions of use*—(1) *Amount.*

(i) For topical dermatological use: Clean affected areas and remove any encrusted discharge or exudate, and apply sparingly either ointment in a thin film.¹

(ii) For otic use: Clean ear canal of impacted cerumen, remove any foreign bodies such as grass awns and ticks, and instill three to five drops of petrolatum base ointment. Preliminary use of a local anesthetic may be advisable.¹

(iii) For infected anal glands and cystic areas: Drain gland or cyst and fill with petrolatum base ointment.¹

(2) *Indications for use.* (i) Topically: Use either ointment in dogs and cats for anti-inflammatory, antipruritic, antifungal, and antibacterial treatment of superficial bacterial infections, and for dermatologic disorders characterized by inflammation and dry or exudative dermatitis, particularly associated with bacterial or candidal (*Candida albicans*) infections.¹

(ii) Otitis, cysts, and anal gland infections: Use petrolatum base ointment in dogs and cats for the treatment of acute and chronic otitis and interdigital cysts, and in dogs for anal gland infections.¹

¹These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

¹These conditions are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

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(3) *Limitations.* For mild inflammations, use once daily to once a week. For severe conditions, apply initially two to three times daily, decreasing frequency as improvement occurs. Not intended for treatment of deep abscesses or deep-seated infections. Not for ophthalmic use. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13873, Mar. 27, 1975, as amended at 43 FR 29770, July 11, 1978; 50 FR 41490, Oct. 11, 1985; 53 FR 39257, Oct. 6, 1988; 54 FR 5431, Feb. 3, 1989]

§ 524.1600b Nystatin, neomycin, thiostrepton, and triamcinolone acetate ophthalmic ointment.

(a) *Specifications.* Each cubic centimeter of ointment contains: 100,000 units of nystatin, neomycin sulfate equivalent to 2.5 milligrams of neomycin base, 2,500 units of thiostrepton, and 1.0 milligram of triamcinolone acetate.

(b) *Sponsor.* See No. 053501 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is recommended for ophthalmic use as an anti-inflammatory, antipruritic, antifungal (*Candida albicans*), and antibacterial ointment for local therapy in keratitis and conjunctivitis in cats and dogs and for infectious keratoconjunctivitis (pink eye) in cattle.

(2) It is to be administered as follows:

(i) For conjunctivitis and keratitis: Apply one drop of ointment to the affected eye(s) two or three times daily. Treatment may be continued for up to 2 weeks if necessary.

(ii) For bovine infectious keratoconjunctivitis: Apply small line of ointment to the affected eye(s) once daily. Treatment may be continued for up to 2 weeks if necessary.

(iii) Frequency of administration is dependent on the severity of the condition. For mild inflammations, applications may range from once daily to once a week; for severe conditions the drug may be applied as often as two to three times daily. Frequency of treat-

data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

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ment may be decreased as improvement occurs.

(3) For use only by or on the order of a licensed veterinarian.

[40 FR 13873, Mar. 27, 1975, as amended at 50 FR 41490, Oct. 11, 1985]

§ 524.1662 Oxytetracycline hydrochloride ophthalmic and topical dosage forms.

§ 524.1662a Oxytetracycline hydrochloride and hydrocortisone spray.

(a) *Specifications.* Each 3-ounce unit of oxytetracycline hydrochloride and hydrocortisone spray contains 300 milligrams of oxytetracycline hydrochloride and 100 milligrams of hydrocortisone with an inert freon propellant such that a 1-second spray treatment will deliver approximately 2.5 milligrams of oxytetracycline hydrochloride and 0.8 milligram of hydrocortisone.

(b) *Sponsor.* See No. 000069 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is indicated for relief of discomfort and continued treatment of many allergic, infectious, and traumatic skin conditions. The indications include prevention of bacterial infections in superficial wounds, cuts, and abrasions, treatment of allergic dermatoses, including urticaria, eczemas, insect bites, and cutaneous drug reactions, infections associated with minor burns and wounds, and nonspecific pruritus in dogs and cats.

(2) A small quantity should be sprayed on the affected surface by holding the container about 6 inches from the area to be treated and pressing the nozzle for 1 or 2 seconds. Only sufficient spray to coat the skin thinly is necessary. The application of small amounts at frequent intervals will give best results. Before treating animals with long or matted hair, it may be necessary to clip the affected area or spread the hairs to allow the medication to contact the skin surface. Relief may be noted following the first or second treatment; however, treatment should not be discontinued too soon after the initial favorable response has been obtained.

(3) Keep away from eyes or other mucous membranes; avoid inhaling.

use with adequate ventilation; in case of deep or puncture wounds or serious burns, consult a veterinarian.

§ 524.1662b Oxytetracycline hydrochloride, polymyxin B sulfate ophthalmic ointment.

(a) *Specifications.* Each gram of the ointment contains oxytetracycline hydrochloride equivalent to 5 milligrams of oxytetracycline and 10,000 units of polymyxin B sulfate.

(b) *Sponsor.* See No. 000069 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used for the prophylaxis and local treatment of superficial ocular infections due to oxytetracycline- and polymyxin-sensitive organisms. These infections include the following: Ocular infections due to streptococci, rickettsiae, *E. coli*, and *A. aerogenes* (such as conjunctivitis, keratitis, pinkeye, corneal ulcer, and blepharitis in dogs, cats, cattle, sheep, and horses); ocular infections due to secondary bacterial complications associated with distemper in dogs; and ocular infections due to bacterial inflammatory conditions which may occur secondary to other infectious diseases in dogs, cats, cattle, sheep, and horses.

(2) It is administered topically to the eye two to four times daily.

(3) Allergic reactions may occasionally occur. Treatment should be discontinued if reactions are severe. If new infections due to nonsensitive bacteria or fungi appear during therapy, appropriate measures should be taken.

§ 524.1742 N-(Mercaptomethyl) phthalimide S-(O,O-dimethyl phosphorodithioate) emulsifiable liquid.

(a) *Specifications.* The emulsifiable liquid contains 11.6 percent N-(mercaptomethyl) phthalimide S-(O,O-dimethyl phosphorodithioate).

(b) *Sponsor.* See Nos. 011536 and 017032 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Methods of application.* Methods of application to control the following conditions on beef cattle:

To control/method of use	Dilution rate (gal. drug, gal. of water)
Grubs:	
Dip	1:60
Pour-on	1:2
Spray	1:49
Lice:	
Dip	1:60
Pour-on	1:2 or 1:5
Spray	1:49 or 1:100
Homflies:	
Dip	1:60
Spray	1:49 or 1:100
Cattle Ticks:	
Dip	1:60 or 1:240
Spray	1:49
Southern cattle ticks:	
Dip	1:60 or 1:240
Spray	1:49
Scabies mites:	
Dip	1:60
Lone Star Ticks:	
Dip	1:60
Spray	1:49 or 1:100

(i) *Dip vat procedure.* (a) Prior to charging vat, empty old contents and thoroughly clean the vat. Dip vats should be calibrated to maintain an accurate dilution. Add water, then drug to the vat according to the dilution rate indicated in the table. Add super phosphate at a rate of 100 pounds per 1,000 gallons of vat solution. Super phosphate is added to control the pH of the solution and ensure vat stability. Super phosphate is usually available at most fertilizer dealers as 0-45-0 or 0-46-0. Stir the dip thoroughly, preferably with a compressed air device; however, any form of thorough mixing is adequate. Re-stir vat contents prior to each use. During the dipping operation, each time the dip's volume is reduced by ¼ to ½ of its initial volume, replenish with water and add the drug at a rate of 1 gallon for each 50 or 200 gallons water added—depending on dilution rate 1:60 or 1:240. Also add super phosphate as necessary to maintain pH between 4.5 and 6.5. Stir well and resume dipping. Repeat replenishment process as necessary. For evaporation, add additional water accordingly. For added water due to rainfall, merely replenish dip with the product according to directions. If overflow occurs, either analyze for drug concentration and adjust accordingly or dispose of vat contents and recharge. Check pH after each ad-

dition of water or super phosphate to assure proper pH controls.

(b) *Dip maintenance.* (1) With use of dip vat tester, dipping may continue as long as the drug concentration is maintained between 0.15 and 0.25 percent, and the dip is not too foul for satisfactory use as indicated by foul odor or excessive darkening (i.e., color changes from beige to very dark brown).

(2) Without use of dip vat tester, vat should be emptied, cleaned, and recharged each time one of the following occurs: When the dip has been charged for 120 days; when the dip becomes too foul for satisfactory use, within the 120-day limit; if the number of animals dipped equals twice the number of gallons of the initial dip volume, within the 120-day limit.

(ii) *Spray method.* To prepare the spray, mix drug with water according to table and stir thoroughly. Apply the fresh mixture as a high-pressure spray, taking care to wet the skin, not just the hair. Apply to the point of "runoff," about 1 gallon of diluted spray per adult animal. Lesser amounts will permit runoff for younger animals.

(iii) *Pour-on method.* Dilute the drug with water according to table by slowly adding water to the product while stirring. Apply 1 ounce of the diluted mixture per 100 pounds of body weight (to a maximum of 8 ounces per head) down the center line of the back.

(2) *Timing of applications for cattle grub control.* For optimum cattle grub control, it is important to treat as soon as possible after the heel fly season, before the grub larvae reach the gullet or spinal canal, as the rapid kill of large numbers of larvae in these tissues may cause toxic side effects, such as bloat, salivation, staggering, and paralysis.

(3) *Treatment regimens.* (i) Control of scabies mites requires two treatments, 10 to 14 days apart.

(ii) Control of Lone Star Ticks and hornflies requires two treatments, 7 days apart.

(4) *Warnings.* The drug is a cholinesterase inhibitor. Do not use this drug on animals simultaneously or within a few days before or after treatment

with or exposure to cholinesterase-inhibiting drugs, pesticides, or chemicals. Do not apply within 21 days of slaughter. For use on beef cattle only. Do not treat sick, convalescent, or stressed cattle, or calves less than 6 months old except in Federal or State eradication programs where immediate treatment of all animals in an infested herd is mandatory. Be sure free access to drinking water is available to cattle prior to dipping. Do not dip excessively thirsty animals. Do not dip animals when overheated. Repeat treatment as necessary but not more often than every 7 to 10 days. Treatment for lice, ticks, hornflies, and scabies mites may be made any time of the year except when cattle grub larvae are in the gullet or spinal canal. Treatment for lice, ticks, and scabies mites may be made any time 7 to 10 days following treatment for grubs. Do not treat grubs when the grub larvae are in the gullet or spinal canal. Do not get in eyes, on skin, or on clothing. Do not breathe spray mist. Wear rubber gloves, goggles, and protective clothing. In case of skin contact, wash immediately with soap and water; if eyes, flush with water. Wash all contaminated clothing with soap and hot water before re-use.

(d) *Related tolerances.* See 40 CFR 180.261.

[40 FR 13873, Mar. 27, 1975, as amended; 46 FR 27914, May 22, 1981; 48 FR 396 Sept. 1, 1983]

§ 524.1880 Prednisolone-neomycin sulf ophthalmic ointment.

(a) *Specifications.* Prednisolone-neomycin sulfate ophthalmic ointment contains 2 milligrams prednisolone and 5 milligrams neomycin sulfate (equivalent to 3.5 milligrams neomycin base) in each gram of ointment.

(b) *Sponsor.* See No. 017030 § 510.600(c) of this chapter.

(c) *Conditions of use.* The drug is recommended for use in superficial ocular inflammations or infections limited to the conjunctiva or the anterior segment of the eye of cats and dogs, such as those associated with allergic reactions or gross irritants. A small quantity of the ointment should be expressed into the conjunctival

four times a day for 7 days. After 7 days, if clinical improvement is not noted, reevaluation of the diagnosis should be considered. All topical ophthalmic preparations containing corticosteroids with or without an antimicrobial agent are contraindicated in the initial treatment of corneal ulcers. They should not be used until the infection is under control and corneal regeneration is well underway. For use only by or on the order of a licensed veterinarian.

§ 524.1881 Prednisolone acetate ophthalmic and topical dosage forms.

§ 524.1881a [Reserved]

§ 524.1881b Prednisolone acetate-neomycin sulfate sterile suspension.

(a) *Specifications.* Prednisolone acetate-neomycin sulfate sterile suspension contains 2.5 milligrams of prednisolone acetate and 5 milligrams of neomycin sulfate (equivalent to 3.5 milligrams of neomycin base) in each milliliter of sterile suspension.

(b) *Sponsor.* See No. 000009 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is indicated for treating infectious, allergic and traumatic keratitis and conjunctivitis, acute otitis externa, and chronic otitis externa in dogs and cats.

(2) For beginning treatment of acute ocular inflammations 1 or 2 drops may be placed in the conjunctival sac 3 to 6 times during a 24 hour period. When improvement occurs, the dosage may be reduced to 1 drop 2 to 4 times daily. In otitis externa, 2 to 6 drops may be placed in the external ear canal 2 or 3 times daily.

(3) All topical ophthalmic preparations containing corticosteroids with or without an anti-microbial agent are contraindicated in the initial treatment of corneal ulcers. They should not be used until infection is under control and corneal regeneration is well underway.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

§ 524.1883 Prednisolone sodium phosphate-neomycin sulfate ophthalmic ointment.

(a) *Specifications.* Prednisolone sodium phosphate-neomycin sulfate ophthalmic ointment contains prednisolone sodium phosphate equivalent to 2.5 milligrams prednisolone 21-phosphate and 5 milligrams neomycin sulfate (equivalent to 3.5 milligrams neomycin base) in each gram of ointment.

(b) *Sponsor.* See No. 000006 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is recommended for use in superficial ocular inflammations or infections limited to the conjunctiva or the anterior segment of the eye of cats and dogs, such as those associated with allergic reactions or gross irritants.¹

(2) A small quantity of the ointment should be expressed into the conjunctival sac 4 times a day (at intervals of 1 to 8 hours) for a few days until there is a favorable response, then the frequency of application may be reduced to twice daily as long as the condition remains under control. Treatment may require from a few days to several weeks.¹

(3) All topical ophthalmic preparations containing corticosteroids with or without an antimicrobial agent are contraindicated in the initial treatment of corneal ulcers. They should not be used until the infection is under control and corneal regeneration is well underway.¹

(4) For use only by or on the order of a licensed veterinarian.¹

§ 524.1982 Proparacaine hydrochloride ophthalmic solution.

(a) *Specifications.* The drug is an aqueous solution containing 0.5 percent proparacaine hydrochloride, 2.45 percent glycerin as a stabilizer, and 0.2 percent chlorobutanol (choral derivative) and 1:10,000 benzalkonium chloride as preservatives.

¹These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

§ 524.2080

(b) *Sponsor*. See No. 053501 in § 510.600(c) of this chapter.

(c) *Special considerations*. The long-term toxicity of proparacaine is unknown. Prolonged use may possibly delay wound healing.

(d) *Conditions of use*. (1) The drug is indicated for use as a topical ophthalmic anesthetic in animals. It is used as an anesthetic in cauterization of corneal ulcers, removal of foreign bodies and sutures from the cornea, and measurement of intraocular pressure (tonometry) when glaucoma is suspected. Local applications may also be used as an aid in the removal of foreign bodies from the nose and ear canal, as an accessory in the examination and treatment of painful otitis, in minor surgery, and prior to catheterization.

(2) It is administered as follows:

(i) For removal of sutures: Instill one to two drops 2 or 3 minutes before removal of stitches.

(ii) For removal of foreign bodies from eye, ear, and nose: For ophthalmic use, instill three to five drops in the eye prior to examination; for otic use, instill five to 10 drops in the ear; for nasal use, instill five to 10 drops in each nostril every 3 minutes for three doses.

(iii) For tonometry: Instill one to two drops immediately before measurement.

(iv) As an aid in treatment of otitis: Instill two drops into the ear every 5 minutes for three doses.

(v) For minor surgery: Instill one or more drops as required.

(vi) For catheterization: Instill two to three drops with a blunt 20-gauge needle immediately before inserting catheter.

(3) For use only by or on the order of a licensed veterinarian.

[40 FR 13873, Mar. 27, 1975, as amended at 50 FR 41490, Oct. 11, 1985]

§ 524.2080 Ronnel emulsifiable concentrate.

(a) *Specifications*. The emulsifiable concentrate contains 33.34 percent ronnel.

(b) *Sponsor*. See No. 011716 in § 510.600(c) of this chapter.

(c) *Generic status*. These conditions of use were reviewed and found effective by FDA before October 10, 1962.

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New animal drug applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(d) *Conditions of use*—(1) *Dosage and indications*. Administer topically as follows:

Indications (species)	Percent ronnel solution	Length of treatment
Demodectic mange (dogs)	1	Every 4 days for at least 30 days. ¹
Sarcoptic mange (dogs)	1	Every 7 to 10 days for 3 applications.
Ticks (dogs)	1	Apply solution; repeat as indicated. ¹
Fleas and lice (dogs); fleas (cats)	0.25	Apply solution; repeat as indicated.
Ear mites (dogs and cats)	1	Apply solution; repeat as indicated.

¹ Topical application may be combined with oral treatment (tablets).

(2) *Limitations*. Prepare fresh solution for each patient. To prepare a 1-percent solution, add 1 ounce (2 tablespoons) of concentrate to a quart of water. Apply thoroughly to entire body of animal except when treating ear mites. Avoid prolonged or repeated contact of concentrate with skin. Ronnel is a cholinesterase inhibitor. Do not use simultaneously or within a few days before or after treatment with or exposure to cholinesterase inhibiting drugs, pesticides, or chemicals. Treat symptomatically. Atropine is an antidote. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[48 FR 15244, Apr. 8, 1983]

§ 524.2101 Selenium disulfide suspension.

(a) *Specifications*. The product contains 0.9-percent weight in weight (w/w) selenium disulfide (1-percent weight in volume (w/v)).

(b) *NAS/NRC status*. These conditions are NAS/NRC reviewed and found effective. NADA's for similar products for these conditions of use need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(c) *Sponsors.* See 000570, 011536, 015563, 017135, and 023851 in § 510.600(c) of this chapter.

(1) *Indications for use.* For use on dogs as a cleansing shampoo and as an agent for removing skin debris associated with dry eczema, seborrhea, and nonspecific dermatoses.

(2) *Amount.* One to 2 ounces per application.

(3) *Limitations.* Use carefully around scrotum and eyes, covering scrotum with petrolatum. Allow the shampoo to remain for 5 to 15 minutes before thorough rinsing. Repeat treatment once or twice a week. If conditions persist or if rash or irritation develops, discontinue use and consult a veterinarian.

(d) *Sponsors.* See 050604 in § 510.600(c) of this chapter.

(1) *Indications for use.* For use on dogs as a cleaning shampoo and as an agent for removing skin debris associated with dry eczema, seborrhea, and nonspecific dermatoses.

(2) *Amount.* One to 2 ounces per application.

(3) *Limitations.* Use carefully around the scrotum and eyes, covering scrotum with petrolatum and instilling boric acid ophthalmic ointment into eyes. Allow shampoo to remain for 5 to 15 minutes before thorough rinsing. Repeat at 4- to 7-day intervals. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

7 FR 53351, Nov. 26, 1962, as amended at 3 FR 32762, July 19, 1983]

524.2140 Squalane, pyrethrins and piperonyl butoxide.

(a) *Specifications.* The drug contains 5 percent squalane (hexamethylteracosane), 0.05 percent pyrethrins and 0.50 percent technical piperonyl butoxide.

(b) *Sponsor.* See No. 017030 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used for the treatment of ear mites in dogs and cats.

(2) It is administered as follows: Cats and dogs 5-15 pounds body weight, 4 to 5 drops in each ear daily. Dogs 16-30 pounds body weight, 5 to 10 drops in each ear daily. Dogs 30 pounds body weight and over 10 to 15 drops in each ear daily. The recommended treat-

ment is for 7 to 10 days with repeated treatment in 2 weeks if necessary.

§ 524.2350 Tolnaftate cream.

(a) *Specifications.* The drug contains 1 percent tolnaftate (2-naphthyl-N-methyl-N-(3-tolyl) thionocarbamate) in an anhydrous cream base.

(b) *Sponsor.* See No. 000061 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is indicated for treatment of ringworm lesions due to *Microsporum canis* and *Microsporum gypseum* in dogs and cats.

(2) A small amount of the cream is applied to the affected areas once or twice a day for 2 to 4 weeks. The areas to be treated are first cleared of exudate and the hair clipped if the areas are not already denuded. The cream is massaged into each lesion and immediate surrounding area until the cream is no longer visible.

(3) If no response is seen after 2 weeks of treatment with the drug the diagnosis should be reviewed.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[43 FR 29289, July 7, 1978, as amended at 52 FR 7833, Mar. 13, 1987]

§ 524.2481 Triamcinolone acetonide cream.

(a) *Specifications.* Triamcinolone acetonide cream contains 0.1 percent triamcinolone acetonide in an aqueous vanishing cream base.

(b) *Sponsor.* See No. 053501 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is recommended for use on dogs as an anti-inflammatory, antipruritic, and antiallergic agent for topical treatment of allergic dermatitis and summer eczema.

(2) The drug is applied by rubbing into affected areas two to four times daily for 4 to 10 days.

(3) For use only by or on the order of a licensed veterinarian.

[40 FR 13873, Mar. 27, 1975, as amended at 50 FR 41490, Oct. 11, 1985]

§ 524.2620

§ 524.2620 Liquid crystalline trypsin, Peru balsam, castor oil.

(a)(1) *Specifications.* The drug is a liquid for direct application or an aerosol preparation formulated so that each gram delivered to the wound site contains 0.12 milligram of crystalline trypsin, 87.0 milligrams of Peru balsam, and 788.0 milligrams of castor oil.

(2) *Sponsor.* See No. 000514 in § 510.600(c) of this chapter.

(b)(1) *Specifications.* The drug is a liquid for direct application or an aerosol preparation formulated so that each gram delivered to the wound site contains 0.1 milligram of crystalline trypsin, 72.5 milligrams of Peru balsam, and 800 milligrams of castor oil.

(2) *Sponsor.* See No. 051268 in § 510.600(c) of this chapter.

(c) *Conditions of use.* The drug is used as an aid in the treatment of external wounds and assists healing by facilitating the removal of necrotic tissue, exudate and organic debris.

[40 FR 13873, Mar. 27, 1975, as amended at 41 FR 56307, Dec. 28, 1976; 50 FR 9800, Mar. 12, 1985]

§ 524.2640 Tylosin, neomycin eye powder.

(a) *Specifications.* Tylosin is the antibiotic substance produced by growth of *Streptomyces fradiae* or the same antibiotic substance produced by any other means. Tylosin, present as the tartrate salt, conforms to the appropriate antibiotic standard. Tylosin contains at least 95 percent tylosin as a combination of tylosin A, tylosin B, tylosin C, and tylosin D of which at least 80 percent is tylosin A as determined by a method entitled "Determination of Factor Content in Tylosin by High Performance Liquid Chromatography," which is incorporated by reference. Copies are available from the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857, or available for inspection at the Office of the Federal Register, 1100 L St. NW., Washington, DC 20408.

(b) *Sponsor.* See No. 000986 in § 510.600(c) of this chapter.

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(c) *Conditions of use.* (1) It is used in cattle for the treatment of pinkeye (infectious keratoconjunctivitis).

(2) It is administered by holding the eyelids open and dusting powder into both eyes. The treatment is repeated daily for up to 7 days depending on the severity of the infection. Affected animals should be protected from direct sunlight, dust, and flies. In an affected herd, all animals with or without signs of the disease should receive at least one treatment.

(3) If there is severe eye damage or if the condition persists or increases, discontinue administering the drug and consult a veterinarian.

[40 FR 13873, Mar. 27, 1975, as amended at 50 FR 49841, Dec. 5, 1985]

PART 526—INTRAMAMMARY DOSAGE FORMS NOT SUBJECT TO CERTIFICATION

Sec.

526.363 Cephapirin benzathine.

526.820 Erythromycin.

526.1590 Novobiocin oil suspension.

AUTHORITY: Sec. 512(i), 82 Stat. 347 (21 U.S.C. 360b(i)); 21 CFR 5.10 and 5.83.

§ 526.363 Cephapirin benzathine.

(a) *Specifications.* Each 10 milliliter disposable syringe contains 300 milligrams of cephapirin activity (as cephapirin benzathine) in a peanut-oil gel.

(b) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See § 556.115 of this chapter.

(d) *Conditions of use—(1) Amount.* Infuse contents of one syringe into each infected quarter.

(2) *Indications for use.* Use in dry cows for treatment of mastitis caused by susceptible strains of *Streptococcus agalactiae* and *Staphylococcus aureus*.

(3) *Limitations.* Infuse each infected quarter following last milking or early in the dry period, but no later than 30 days before calving. Milk from treated cows must not be used for food during the first 72 hours after calving. Animals infused with this product must not be slaughtered for food until 48 days after the latest infusion. For use in dry cows only.

[43 FR 37174, Aug. 22, 1978, as amended at 53 FR 27851, July 25, 1988]

§ 526.820 Erythromycin.

(a) *Specifications.* (1) Each 6-milliliter, single-dose, disposable syringe contains 300 milligrams of erythromycin (as the base), 0.45 milligram of butylated hydroxyanisole, and 0.45 milligram of butylated hydroxytoluene.

(2) Each 12-milliliter, single-dose, disposable syringe contains 600 milligrams of erythromycin (as the base), 0.90 milligram of butylated hydroxyanisole, and 0.90 milligram of butylated hydroxytoluene.

(3) The vehicle is triglyceride of saturated fatty acids from coconut oil.

(4) The drug may or may not be sterile.

(b) *Sponsor.* See No. 050604 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.*

(i) *Lactating cows:* After milking, cleaning, and disinfecting, infuse contents of a single 6-milliliter syringe into each infected quarter; repeat procedure at 12-hour intervals for a maximum of 3 consecutive infusions.

(ii) *Dry cows:* After milking, cleaning, and disinfecting, infuse contents of a single 12-milliliter syringe into each infected quarter at the time of drying off.

(2) *Indications for use.* Treatment of mastitis due to *Staphylococcus aureus*, *Streptococcus agalactiae*, *Streptococcus dysgalactiae*, and *Streptococcus uberis* in lactating or dry cows.

(3) *Limitations.* Milk taken from animals during treatment and for 36 hours (3 milkings) after the latest treatment must not be used for food.

[43 FR 15772, Apr. 13, 1982]

§ 526.1590 Novobiocin oil suspension.

(a)(1) *Specifications.* Each 10 milliliters of oil suspension contains the equivalent of 400 milligrams of novobiocin (present as sodium novobiocin).

(2) *Sponsor.* See No. 000009 in § 510.600(c) of this chapter.

(3) *Related tolerances.* See § 556.460 of this chapter.

(4) *Conditions of use—(1) Amount.* Ten milliliters (equivalent to 400 milligrams of novobiocin) infused in each quarter.

(ii) *Indications for use.* It is used in dry cows for the treatment of mastitis caused by susceptible strains of *Staphylococcus aureus* and *Streptococcus agalactiae*.

(iii) *Limitations.* Infuse each quarter at the time of drying off, but not less than 30 days prior to calving. Do not slaughter treated animals for food use for 30 days following udder infusion. For udder installation for the treatment of mastitis in dry cows only.

(b)(1) *Specifications.* Each 10 milliliters of oil suspension contains the equivalent of 150 milligrams of novobiocin (present as sodium novobiocin).

(2) *Sponsor.* See No. 000009 in § 510.600(c) of this chapter.

(3) *Related tolerances.* See § 556.460 of this chapter.

(4) *Conditions of use—(i) Amount.* Infuse 10 milliliters (equivalent to 150 milligrams of novobiocin) in each quarter after milking. Repeat treatment once after 24 hours.

(ii) *Indications for use.* Use in lactating cows for treatment of mastitis caused by susceptible strains of *Staphylococcus aureus*.

(iii) *Limitations.* Do not milk for at least 6 hours after treatment; afterwards, milk at regular intervals. Milk taken from treated animals within 72 hours (6 milkings) after latest treatment must not be used for food. Do not slaughter treated animals for food for 15 days following latest treatment. If redness, swelling, or abnormal milk persists or increases after treatment, discontinue use and consult a veterinarian. For udder instillation in lactating cattle only. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[43 FR 10554, Mar. 14, 1978]

PART 529—CERTAIN OTHER DOSAGE FORM NEW ANIMAL DRUGS NOT SUBJECT TO CERTIFICATION

Sec.

529.50 Amikacin sulfate intrauterine solution.

529.360 Cephalothin discs.

529.365 Cephapirin sodium for intramammary infusion.

529.400 Chlorhexidine tablets and suspension.

§ 529.50

Sec.

- 529.810 Enflurane.
- 529.1003 Flurogestone acetate-impregnated vaginal sponge.
- 529.1030 Formalin solution.
- 529.1044 Gentamicin sulfate in certain other dosage forms.
- 529.1044a Gentamicin sulfate intrauterine solution.
- 529.1044b Gentamicin sulfate solution.
- 529.1115 Halothane.
- 529.1186 Isoflurane.
- 529.1528 Nifurpirinol capsules.
- 529.2090 Salicylic acid.
- 529.2503 Tricaine methanesulfonate.

AUTHORITY: Sec. 512(i), 82 Stat. 347 (21 U.S.C. 360b(i)); 21 CFR 5.10 and 5.83.

SOURCE: 40 FR 13881, Mar. 27, 1975, unless otherwise noted.

§ 529.50 Amikacin sulfate intrauterine solution.

(a) *Specifications.* Each milliliter of sterile aqueous solution contains 250 milligrams of amikacin (as the sulfate).

(b) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* Two grams (8 milliliters) diluted with 200 milliliters of sterile physiological saline per day for 3 consecutive days.

(2) *Indications for use.* For treating genital tract infections (endometritis, metritis, and pyometra) in mares when caused by susceptible organisms including *E. coli*, *Pseudomonas* spp., and *Klebsiella* spp.

(3) *Limitations.* For intrauterine infusion in the horse only. Not for use in horses intended for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[48 FR 9640, Mar. 8, 1983, as amended at 53 FR 27852, July 25, 1988]

§ 529.360 Cephalothin discs.

(a) *Specifications.* Cephalothin discs, comply with the requirements of § 460.1 of this chapter.

(b) *Sponsor.* See No. 000986 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The discs are used for determining the in vitro susceptibility of bacteria to cephaloridine and cephalonium.

(2) For veterinary laboratory diagnosis only.

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§ 529.365 Cephapirin sodium for intramammary infusion.

(a) *Specifications.* Each 10-milliliter dose contains 200 milligrams of cephapirin sodium activity in a peanut-oil gel.

(b) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See § 556.115 of this chapter.

(d) *Conditions of use.* (1) The drug is used for the treatment of lactating cows having bovine mastitis caused by susceptible strains of *Streptococcus agalactiae* and *Staphylococcus aureus*.

(2) Administer one dose into each infected quarter immediately after the quarter has been completely milked out. Do not milk out for 12 hours. Repeat once only in 12 hours. If improvement is not noted within 48 hours after treatment, consult your veterinarian.

(3) Milk that has been taken from animals during treatment and for 96 hours (8 milkings) after the last treatment must not be used for food. Treated animals must not be slaughtered for food until 4 days after the last treatment.

[40 FR 57455, Dec. 10, 1975, as amended at 53 FR 27852, July 25, 1988]

§ 529.400 Chlorhexidine tablets and suspension.

(a) *Specification.* Each tablet and each 28-milliliter syringe of suspension contain 1 gram of chlorhexidine dihydrochloride.¹

(b) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Amount.* Place 1 or 2 tablets deep in each uterine horn; or infuse a solution of 1 tablet dissolved in an appropriate amount of clean boiled water; or infuse one syringe of suspension into the uterus.¹

(2) *Indications for use.* For prevention or treatment of metritis and vagi-

¹ These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

nititis in cows and mares when caused by pathogens sensitive to chlorhexidine dihydrochloride.¹

(3) *Limitations.* Prior to administration, remove any unattached placental membranes, any excess uterine fluid or debris, and carefully clean external genitalia. Use a clean, sterile inseminating pipette for administering solutions and suspensions. Treatment may be repeated in 48 to 72 hours.¹

[43 FR 10705, Feb. 23, 1979]

§ 529.810 Enflurane.

(a) *Specifications.* The drug is a clear, colorless, nonflammable, nonexplosive liquid.

(b) *Sponsor.* See 010019 in § 510.600(c) of this chapter.

(c) *Conditions for use—(1) Amount.* For induction of surgical anesthesia: 4 to 5 percent enflurane (with oxygen) for 10 to 15 minutes. For maintenance of surgical anesthesia: 2.2 to 3.5 percent enflurane (with oxygen).

(2) *Indications for use.* For induction and maintenance of general anesthesia in horses.

(3) *Limitations.* Administer by inhalation; not for use in horses sensitive to halogenated anesthetics; increasing depth of anesthesia may produce muscle twitching, particularly about face, neck, and forelimb; not for use in pregnant mares, foals or weanlings; use less than usual amounts of nondepolarizing muscle relaxants with enflurane; not for use in horses intended for food; observe all customary precautions for use of vasoconstrictor substances; Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[46 FR 18965, Mar. 27, 1981, as amended at 49 FR 13494, Apr. 5, 1984]

§ 529.1003 Fluorogestone acetate-impregnated vaginal sponge.

(A) *Specifications.* Each vaginal sponge contains 20 milligrams of fluorogestone acetate.

(b) *Sponsor.* See No. 000014 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Indications for use.* For synchronizing estrus/ovulation in cycling adult ewes during their normal breeding season.

(2) *Limitations.* Using applicator provided, insert sponge into ewe's vagina 13 days before desired start of breeding. For intravaginal use in sheep only. Do not use in young ewes that have not had lambs. Use plastic or rubber gloves when handling large numbers of sponges to minimize exposure to drug. Do not leave sponge in the vagina for more than 21 days. Ewes must not be slaughtered for food within 30 days of sponge removal.

[49 FR 45420, Nov. 16, 1984]

§ 529.1030 Formalin solution.

(a) *Specifications.* Formalin solution is an aqueous solution containing approximately 37 percent by weight of formaldehyde gas, U.S.P.

(b) *Sponsor.* See Nos. 049968 and 051212 in § 510.600(c) of this chapter.

(c) *Conditions of use—(1) Indications for use.* The drug is added to the environmental water as follows:

(i) For control of the protozoa: *Ichthyophthirius* spp., *Chilodonella* spp., *Costia* spp., *Scyphidia* spp., *Epistylis* spp., and *Trichodina* spp.; and the monogenetic trematodes: *Cleidodiscus* spp., *Gyrodactylus* spp., and *Dactylogyrus* spp. on salmon, trout, catfish, largemouth bass, and bluegill.

(ii) For control of fungi of the family Saprolegniaceae on salmon, trout, and esocid eggs.

(2) *Amount.* The drug concentrations required are as follows:

(i) For control of external parasites on fish:

Fish	Concentration of formalin (microliters per liter)	
	Tanks and raceways (for up to 1 hour)	Earthen ponds (indefinitely)
Salmon and trout:		
Above 50 °F.....	Up to 170.....	15-25
Below 50 °F.....	Up to 250.....	15-25
Catfish, largemouth bass, and bluegill.	Up to 250.....	15-25

¹ Use the lower concentrations when pond is heavily loaded with fish or phytoplankton.

(ii) For control of fungi of the Saprolegniaceae on salmon, trout, and esocid eggs: Apply in constant flow water supply of incubating facilities for 15 minutes. Concentration of for-

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malin used is 1,000 to 2,000 microliters per liter.

(d) *Limitations.* Fish tanks and raceways may be treated daily until parasite control is achieved. Pond treatment may be repeated in 5 to 10 days if needed. However, pond treatments for *Ichthyophthirius* should be made at 2-day intervals until control is achieved. Egg tanks may be treated as often as necessary to prevent growth of fungi. Do not use formalin which has been subjected to temperatures below 40 °F, or allowed to freeze. Do not treat ponds containing striped bass. Treatments in tanks should never exceed 1 hour even if fish show no signs of stress. Do not apply formalin to ponds with water warmer than 27 °C (80 °F), when a heavy bloom of phytoplankton is present, or when the concentration of dissolved oxygen is less than 5 milligrams per liter.

[51 FR 11441, Apr. 3, 1986, as amended at 54 FR 5432, Feb. 3, 1989]

§ 529.1044 Gentamicin sulfate in certain other dosage forms.

§ 529.1044a Gentamicin sulfate intrauterine solution.

(a) *Specifications.* Each milliliter of the drug contains 50 or 100 milligrams of gentamicin (as the sulfate) in sterile aqueous solution.

(b) *Sponsor.* See No. 000061, in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is indicated for use for control of bacterial infections of the uterus in horses (metritis) and as an aid in improving conception in mares with uterine infections caused by bacteria sensitive to gentamicin.

(2) It is administered at a dosage level of 2 to 2.5 grams per day for 3 to 5 days during estrus, each dose being diluted with 200 to 500 milliliters of sterile physiological saline before aseptic infusion into the uterus.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(4) Not for use in horses intended for food.

[40 FR 13881, Mar. 27, 1975, as amended at 40 FR 48676, Oct. 17, 1975; 48 FR 31386, July 8, 1983; 52 FR 7833, Mar. 13, 1987]

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§ 529.1044b Gentamicin sulfate solution.

(a) *Specifications.* Each milliliter of solution contains gentamicin sulfate equivalent to 50 milligrams of gentamicin base.

(b) *Sponsor.* See No. 000061 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is recommended as an aid in the reduction or elimination of the following microorganisms from turkey-hatching eggs: *Arizona hinshawii* (paracolon), *Salmonella st. paul*, and *Mycoplasma meleagridis*.

(2) The drug is added to clean water to provide a dip solution with a gentamicin concentration of 250 to 1,000 parts per million. A concentration of 500 parts per million is recommended. Clean eggs should be held submerged in the gentamicin solution under a vacuum of about 27.5 to 38 centimeters of mercury for 5 minutes followed by additional soaking in gentamicin solution for approximately 10 minutes at atmospheric pressure. Eggs can also be treated by warming them for 3 to 6 hours at approximately 100° F. then immediately submerging them in gentamicin solution maintained at about 40° F., keeping the eggs submerged for 10 to 15 minutes.

(3) For use in the dipping treatment of turkey-hatching eggs only. Eggs which have been dipped in the drug shall not be used for food.

[40 FR 13881, Mar. 27, 1975, as amended at 52 FR 7833, Mar. 13, 1987]

§ 529.1115 Halothane.

(a) *Specifications.* The drug is a colorless, odorless, nonflammable, nonexplosive, heavy liquid containing 0.01 percent thymol as a preservative.

(b) *Sponsor.* See 000856 in § 510.600(c) of this chapter.

(c) *Conditions of use.*—(1) *Amount.* Two to 5 percent of inhaled atmosphere for induction of anesthesia; 0.5 to 2 percent for maintenance of anesthesia.¹

¹These conditions have been reviewed by FDA and found effective. NADA's for similar products for these conditions of use need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(2) *Indications for use.* For nonfood animals for the induction and maintenance of anesthesia.¹

(3) *Limitations.* Administered by inhalation. May be administered with either oxygen or a mixture of oxygen and nitrous oxide. Place drug vaporizer between the gas supply and breathing bag to prevent overdosage. Not recommended for obstetrical anesthesia except when uterine relaxation is required. Do not use in pregnant animals; information on possible adverse effects on fetal development is not available. Operating rooms should have adequate ventilation to prevent accumulation of anesthetic gases. Not for use in animals intended for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

46 FR 27915, May 22, 1981

§ 529.1186 Isoflurane.

(a) *Specifications.* The drug is a clear, colorless, stable liquid containing no additives or chemical stabilizers. It is nonflammable and nonexplosive.

(b) *Sponsor.* See No. 010019 in § 510.600(c) of this chapter.

(c) *Conditions of use.*—(1) *Amount.* For induction of surgical anesthesia: 3 to 5 percent isoflurane (with oxygen) for 5 to 10 minutes. For maintenance of surgical anesthesia: 1.5 to 1.8 percent isoflurane (with oxygen).

(2) *Indications for use.* For induction and maintenance of general anesthesia in horses.

(3) *Limitations.* Administer by inhalation; not for use in horses sensitive to halogenated agents; increasing depth of anesthesia may increase hypotension and respiratory depression; use less than usual amounts of nondepressing relaxants; use with vaporizers producing predictable percentage concentrations; not for use in horses intended for food; Federal law restricts this drug to use by or on the order of a licensed veterinarian.

1 FR 594, Jan. 7, 1986

§ 529.1526 Nifurpirinol capsules.

(a) *Specifications.* Each capsule contains 3.8 or 7.6 milligrams of nifurpirinol.

(b) *Sponsor.* See No. 043731 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used in treating aquarium fish for the control of columnaris disease caused by *Chondrococcus columnaris* susceptible to nifurpirinol.

(2) Use one 3.8 milligram nifurpirinol capsule for each 10 gallons of aquarium water. Empty the contents of the capsule directly into the water and stir briefly. Treat for at least 1 hour. If activated charcoal or carbon filtration is being used, disconnect during treatment, but maintain adequate aeration. Resume water filtration after 1 hour treatment. Usually a single treatment is sufficient. For aquariums with charcoal filters, nifurpirinol can be used once each 24 hours up to 3 consecutive days, discontinuing filtration during treatment. If aquarium does not have charcoal filter, do not retreat within 5 days.

(3) Do not use in salt water aquariums.

(4) Do not use while egg bearers or live bearers are reproducing.

[40 FR 60052, Dec. 31, 1975, as amended at 47 FR 20758, May 14, 1982]

§ 529.2090 Salicylic acid.

(a) *Specifications.* (1) Each dose contains 0.55 gram of salicylic acid in a gum arabic and dextrin vehicle.

(2) Each dose is incorporated upon a device (teat dilator) suitable for insertion into and subsequent removal from the teat canal.

(b) *Sponsor.* See No. 035999 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) The drug is used for the removal of scar tissue in the teat canal of milk-producing cows.

(2) The labeling bears directions to the user to:

(i) Treat lactating cows initially by inserting dosage and removal of the device;

(ii) Insert second dose and permit device to remain in canal until the next milking; and

(iii) Insert one dose following each milking for not more than 2 days.

(3) Milk that has been drawn from animals within 48 hours of such treatment may not be used for food.

§ 529.2503

[41 FR 10984, Mar. 15, 1976, as amended at 43 FR 29290, July 7, 1978]

§ 529.2503 Tricaine methanesulfonate.

(a) *Chemical name.* Ethyl-m-amino-benzoate methanesulfonate.

(b) *Sponsor.* See No. 051212 in § 510.600(c) of this chapter.

(c) *Conditions of use.* (1) It is used for the temporary immobilization of fish, amphibians, and other aquatic coldblooded animals (poikilotherms) as an aid in handling during manual spawning (fish stripping), weighing, measuring, marking, surgical operations, transport, photography, and research.

(2) It is used as follows:

(i) For fish the drug is added to ambient water at a concentration of from 15 to 330 milligrams per liter depending upon the degree of anesthetization or sedation desired, the species and size of the fish, and the temperature and softness of the water. Preliminary tests of solutions must be made with small numbers of fish to determine the desired rates of sedation or anesthesia and the appropriate exposure times for the specific lots of fish under prevailing conditions.

(ii) For amphibians and other aquatic coldblooded animals, the drug is added to ambient water in concentrations of from 1:1000 to 1:20,000 depending upon species and stage of development.

(iii) Do not use within 21 days of harvesting fish for food. Use in fish intended for food should be restricted to Ictaluridae, Salmonidae, Esocidae, and Percidae, and water temperature should exceed 10° C. (50° F.). In other fish and in cold-blooded animals, the drug should be limited to hatchery or laboratory use.

[40 FR 13881, Mar. 27, 1975, as amended at 49 FR 5748, Feb. 15, 1984; 51 FR 11439, Apr. 3, 1986]

PART 536—TESTS FOR SPECIFIC ANTIBIOTIC DOSAGE FORMS

Sec.

536.500 Penicillin bougies.

536.501 Penicillin-streptomycin ointment; penicillin-dihydrostreptomycin ointment.

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536.502 Penicillin-streptomycin bougies; penicillin-dihydrostreptomycin bougies.

536.503 Penicillin-bacitracin ointment.

536.504 Crystalline penicillin and bacitracin.

536.505 Penicillin-streptomycin-bacitracin ointment; penicillin-dihydrostreptomycin-bacitracin ointment; penicillin-streptomycin-bacitracin methylene disalicylate ointment; penicillin-dihydrostreptomycin-bacitracin methylene disalicylate ointment.

536.506 Penicillin-bacitracin-neomycin ointment; penicillin-bacitracin-neomycin in oil.

536.507 Procaine penicillin and benzathine penicillin G in streptomycin sulfate solution; procaine penicillin and benzathine penicillin G in dihydrostreptomycin sulfate solution (procaine penicillin and benzathine penicillin G in crystalline dihydrostreptomycin sulfate solution).

536.508 Procaine penicillin-streptomycin-polymyxin in oil; procaine penicillin-dihydrostreptomycin-polymyxin in oil; procaine penicillin-streptomycin-polymyxin ointment; procaine penicillin-dihydrostreptomycin-polymyxin ointment.

536.509 Penicillin-streptomycin-erythromycin ointment; penicillin-dihydrostreptomycin-erythromycin ointment.

536.510 Penicillin-tetracycline phosphate complex-novobiocin-nystatin capsules.

536.511 Penicillin-streptomycin-bacitracin methylene disalicylate-neomycin ointment; penicillin-dihydrostreptomycin-bacitracin methylene disalicylate-neomycin ointment.

536.512 Procaine penicillin G-novobiocin-neomycin-dihydrostreptomycin in oil.

536.513 Streptomycin/dihydrostreptomycin for inhalation therapy.

536.514 Streptomycin sulfate/dihydrostreptomycin sulfate oral powder.

536.515 Dihydrostreptomycin-neomycin-polymyxin aerosol solution.

536.516 Chlortetracycline-neomycin-streptomycin/dihydrostreptomycin penicillin ointment; tetracycline hydrochloride-neomycin-streptomycin/dihydrostreptomycin penicillin ointment.

536.517 Calcium chlortetracycline-neomycin sulfate mastitis suspension.

AUTHORITY: Secs. 507, 512, 59 Stat. 483 as amended, 82 Stat. 343-351 (21 U.S.C. 351, 360b); 21 CFR 5.10, 5.83.

SOURCE: 40 FR 13882, Mar. 27, 1975, unless otherwise noted.

§ 536.500 Penicillin bougies.

(a) *Potency.* Proceed as directed in § 440.180a(b)(1) of this chapter.

(b) *Moisture.* Proceed as directed in § 436.500(c) of this chapter, using 1.0 to 2.0 grams of bougies dissolved in 10 milliliters of dry chloroform if it contains the excipient polyethylene glycol. If it does not contain the excipient polyethylene glycol, proceed as directed in § 440.80a(b)(5)(i) of this chapter.

§ 536.501 Penicillin-streptomycin ointment; penicillin-dihydrostreptomycin ointment.

(a) *Potency*—(1) *Total penicillin content.* Proceed as directed in § 440.380a(b)(1) or § 440.80a(b)(5)(iv)(a) of this chapter, except that if the iodometric chemical assay described in § 440.80a(b)(5)(iv)(a) of this chapter is used prepare the sample as follows: Accurately measure two representative portions of the sample, each equivalent to about 20,000 units. Place one portion in a centrifuge tube containing 10.0 milliliters of 1 percent phosphate buffer, pH 6.0, and 10.0 milliliters of chloroform for each 5 milliliters or grams of sample. Shake the tube for 1 minute and centrifuge to obtain a substantially clear buffer layer. Use 2.0 milliliters of this solution as the blank. Add one drop of 1.2 N HCl to the blank immediately before the addition of the 10.0 milliliters of 0.01 N I₂. Immediately titrate with 0.01 N Na₂S₂O₃. Place the second portion of the sample in a centrifuge tube containing 10.0 milliliters of 1 N NaHCO₃ (previously adjusted to a pH of 9.3±0.2 with 1.0 N NaOH) and 10.0 milliliters of chloroform for each 5 milliliters or grams of sample. Shake the tube for 1 minute and centrifuge to obtain a substantially clear aqueous layer. To 2.0 milliliters of the aqueous layer, add 2.0 milliliters of 1 N NaOH and allow to stand for 15 minutes. Add sufficient 1.2 N HCl to obtain a pH of 9.0, then add 10.0 milliliters of 0.01 N I₂. Allow to stand for 15 minutes and then titrate with 0.01 N Na₂S₂O₃. From the titration data calculate the amount of penicillin in the sample. Its content of penicillin is satisfactory if it contains not less than 85 percent of

the number of units that it is represented to contain.

(2) *Crystalline sodium penicillin or potassium penicillin content*—(1) *Direct method*—(a) *Preparation of the solution for assay.* Accurately measure a representative portion of the sample equivalent to about 20,000 units of crystalline sodium penicillin or potassium penicillin and place it in a centrifuge tube containing 10.0 milliliters of 20 percent sodium sulfate solution and 10.0 milliliters of chloroform for each 5 milliliters or grams of sample. Shake the tube for 1 minute and then centrifuge to obtain a substantially clear aqueous layer. This is used as the solution for assay.

(b) *Iodometric assay for total penicillin in the solution for assay.* Determine the quantity of penicillin in the solution for assay by the iodometric assay procedure described in § 440.80a(b)(5)(iv)(a), of this chapter.

(c) *Colorimetric determination of procaine penicillin in the solution for assay.* (1) If the sample does not contain sulfonamides, determine the procaine penicillin in the solution for assay by the colorimetric procedure described in § 436.503(b)(3) of this chapter.

(2) If the sample contains sulfonamides, proceed as follows: Place 10.0 milliliters of the solution for assay in a separatory funnel containing 2 milliliters of 1 N NaOH and 10.0 milliliters of chloroform and shake for 1 minute. Allow the layers to separate and collect the lower chloroform layer in a cylinder containing 10.0 milliliters of 4 N HCl. Shake for 1 minute and allow the layers to separate. Using the upper acid layer as the solution for assay, determine the procaine penicillin content by the colorimetric procedure described in § 436.503(b)(3) of this chapter.

(d) The content of crystalline sodium or potassium penicillin in the sample is calculated as follows:

$$A = (B - C)F$$

where:

A=crystalline sodium penicillin or potassium penicillin content of the sample.

B=total number of units of penicillin per milliliter as determined in paragraph (a)(2)(i)(b) of this section.

C=number of units of procaine penicillin per milliliter as determined in paragraph (a)(2)(i)(c) of this section.

F=appropriate dilution factor depending on the dilution made in the preparation of the solution for assay and the size of the representative portion of the sample tested.

(ii) *Indirect method.* The content of crystalline sodium or potassium penicillin is the difference between the total penicillin content determined in paragraph (a)(1) of this section and the procaine penicillin determined in paragraph (a)(3)(i) of this section. Its content of crystalline sodium penicillin or potassium penicillin is satisfactory if it contains not less than 85 percent of the number of units that it is represented to contain.

(3) *Procaine penicillin content*—(i) *Direct method.* Using the stock solution prepared for bioassay in paragraph (a)(1) of this section, determine the procaine penicillin content colorimetrically as directed in paragraph (a)(2)(i)(c)(2) of this section.

(ii) *Indirect method.* The procaine penicillin content of the sample is the difference between the total penicillin content determined in paragraph (a)(1) of this section and the crystalline sodium penicillin or potassium penicillin content determined in paragraph (a)(2) of this section. Its content of procaine penicillin is satisfactory if it contains not less than 85 percent of the number of units that it is represented to contain.

(4) *Streptomycin content.* Proceed as directed in § 444.70a(b)(1) of this chapter, except paragraph (b)(1)(xi) of that section, and in lieu of the directions in § 444.70a(b)(1)(v) and (x)(c), test a representative portion of the sample (usually approximately 1 gram, accurately weighed) or the entire contents of a single-dose container prepared by one of the following methods:

(i) *To assay by the cup-plate method.* Use either extraction or blending.

(a) *Extraction.* Place the sample in a separatory funnel containing approximately 50 milliliters of peroxide-free

ether. If the sample consists of substantially more than 1 gram, use 100 milliliters of ether. Shake the sample and ether until homogeneous. Add 20 milliliters of 0.1 M potassium phosphate buffer, pH 8.0, and shake. If the sample consists of substantially more than 1 gram, use 50 milliliters of buffer. Allow the layers to separate. Remove the buffer layer and repeat the extraction with new portions of buffer at least three times and any additional times necessary to ensure complete extraction of the antibiotic. Combine the extractives and make up to an appropriate measured volume with buffer. To a suitable aliquot add sufficient penicillinase and let stand for 30 minutes at 37° C. to inactivate the penicillin. After inactivation, make the proper estimated dilution with buffer at pH 8.0.

(b) *Blending.* Place the sample in a blending jar containing 1.0 milliliter of 10-percent aqueous solution of polysorbate 80 and sufficient 0.1 M potassium phosphate buffer, pH 8.0, to give a final volume of 500 milliliters. Using a highspeed blender, blend the mixture for 3 minutes. To a suitable aliquot, add sufficient penicillinase and let stand for 30 minutes at 37° C. to inactivate the penicillin. After inactivation, make the proper estimated dilutions with buffer at pH 8.0.

(ii) *To assay by the turbidimetric method.* Place the sample in a separatory funnel containing approximately 50 milliliters of peroxide-free ether. If the sample consists of substantially more than 1 gram, use 100 milliliters of ether. Shake the sample and ether until homogeneous. Add 20 milliliters of distilled water, and shake. If the sample consists of substantially more than 1 gram, use 50 milliliters of water. Allow the layers to separate. Remove the aqueous layer and repeat the extraction with new portions of water at least three times and any additional times necessary to ensure complete extraction of the antibiotic. Combine the extractives, and make up to an appropriate measured volume with water. Remove the aliquot and, if the ratio of the content of penicillin to the content of streptomycin is equal to or greater than one unit for each microgram, add sufficient penicillinase and

let stand for 30 minutes at 37° C. to inactivate the penicillin. Make the proper estimated dilutions with distilled water. Its content of streptomycin is satisfactory if it contains not less than 85 percent of the number of milligrams that it is represented to contain.

(5) *Dihydrostreptomycin content.* Proceed as directed in paragraph (a)(4) of this section, using the dihydrostreptomycin working standard as a standard of comparison. Its content of dihydrostreptomycin is satisfactory if it contains not less than 85 percent of the number of milligrams per gram of ointment that it is represented to contain.

(b) *Moisture.* Proceed as directed in § 540.380a(b)(2) of this chapter.

§ 536.502 Penicillin-streptomycin bougies; penicillin-dihydrostreptomycin bougies.

(a) *Potency—(1) Penicillin content.* Proceed as directed in § 440.180a(b)(1) of this chapter, except the last sentence of that paragraph. Its content of penicillin is satisfactory if it contains not less than 85 percent of the number of units that it is represented to contain.

(2) *Streptomycin content.* Using 12 bougies, proceed as directed in § 444.70a(b)(1) of this chapter, except paragraph (b)(1)(xi) of that section, and if the cup-plate method is used, use potassium phosphate buffer (pH 7.8–8.0) for dissolving the sample in lieu of sterile distilled water as directed in § 444.70a(b)(1)(v) of this chapter and add sufficient penicillinase to the solution under test to completely inactivate the penicillin present. If the turbidimetric method is used, inactivation with penicillinase is not necessary unless the ratio of the content of penicillin to the content of streptomycin is equal to or greater than 1.0 unit for each microgram. Its content of streptomycin is satisfactory if it contains not less than 85 percent of the number of milligrams that it is represented to contain.

(3) *Dihydrostreptomycin content.* Proceed as directed in paragraph (a)(2) of this section, using the dihydrostreptomycin working standard as a standard of comparison. Its content of dihydrostreptomycin is satisfactory

if it contains not less than 85 percent of the number of milligrams it is represented to contain.

(b) *Moisture.* Proceed as directed in § 536.500(b).

§ 536.503 Penicillin-bacitracin ointment.

The requirements for certification and the tests and methods of assay for penicillin-bacitracin ointment are described under § 436.504 of this chapter.

§ 536.504 Crystalline penicillin and bacitracin.

The requirements for certification and the tests and methods of assay for crystalline penicillin and bacitracin are described under § 440.280c of this chapter.

§ 536.505 Penicillin-streptomycin-bacitracin ointment; penicillin-dihydrostreptomycin-bacitracin ointment; penicillin-streptomycin-bacitracin methylene disalicylate ointment; penicillin-dihydrostreptomycin-bacitracin methylene disalicylate ointment.

The requirements for certification and the tests and methods of assay for penicillin-streptomycin-bacitracin ointment; penicillin dihydrostreptomycin-bacitracin ointment; penicillin-streptomycin-bacitracin methylene disalicylate ointment; penicillin-dihydrostreptomycin-bacitracin methylene disalicylate ointment are described under § 436.505 of this chapter.

§ 536.506 Penicillin-bacitracin-neomycin ointment; penicillin-bacitracin-neomycin in oil.

The requirements for certification and the tests and methods of assay for penicillin-bacitracin-neomycin ointment; penicillin-bacitracin-neomycin in oil are described under § 436.508 of this chapter.

§ 536.507 Procaine penicillin and benzathine penicillin G in streptomycin sulfate solution; procaine penicillin and benzathine penicillin G in dihydrostreptomycin sulfate solution (procaine penicillin and benzathine penicillin G in crystalline dihydrostreptomycin sulfate solution).

(a) *Potency—(1) Total potency and procaine penicillin content.* Proceed

§ 536.508

as directed in § 436.507(a) (1) and (2), except that in the iodometric assay one drop of 1.2 *N* HCl is added to the blank immediately, before the addition of the 0.01 *N* iodine.

(2) *Benzathine penicillin G content.* The difference between the total penicillin potency and the procaine penicillin content determined under paragraph (a)(1) of this section represents the benzathine penicillin G content. The benzathine penicillin G content is satisfactory if it is not less than 85 percent of that which it is represented to contain.

(3) *Streptomycin content.* Proceed as directed in § 444.70a(b)(1)(x) and (xi) of this chapter.

(4) *Dihydrostreptomycin content.* Proceed as directed in § 444.10a(b)(1) of this chapter.

(b) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(2) of that section, except use medium C in lieu of medium A, and medium F in lieu of medium E. During the period of incubation, shake the tubes at least once daily.

(c) [Reserved]

(d) *Pyrogens.* Proceed as directed in § 540.250(b)(4) of this chapter.

(e) *pH.* Proceed as directed in § 440.80a(b)(5)(ii) of this chapter, using the undiluted aqueous suspension.

[40 FR 13882, Mar. 27, 1975, as amended at 50 FR 19921, May 13, 1985]

§ 536.508 Procaine penicillin-streptomycin-polymyxin in oil; procaine penicillin-dihydrostreptomycin-polymyxin in oil; procaine penicillin-streptomycin-polymyxin ointment; procaine penicillin-dihydrostreptomycin-polymyxin ointment.

The requirements for certification and the tests and methods of assay for procaine penicillin-streptomycin-polymyxin in oil; procaine penicillin-dihydrostreptomycin-polymyxin in oil; procaine penicillin-streptomycin-polymyxin ointment; procaine penicillin-dihydrostreptomycin-polymyxin ointment are described under § 436.509 of this chapter.

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§ 536.509 Penicillin-streptomycin-erythromycin ointment; penicillin-dihydrostreptomycin-erythromycin ointment.

The requirements for certification and the tests and methods of assay for penicillin-streptomycin-erythromycin ointment; penicillin-dihydrostreptomycin-erythromycin ointment are described under § 436.510 of this chapter.

§ 536.510 Penicillin-tetracycline phosphate complex-novobiocin-nystatin capsules.

(a) *Potency*—(1) *Penicillin content.* Proceed as directed in § 440.180d(b)(1)(i)(a), except in lieu of the directions prescribed in § 440.180d(b)(1)(i)(a)(1) of this chapter, prepare the stock solution by blending 3 capsules in 100 milliliters of potassium phosphate buffer, pH 8.0, using a glass jar and a high-speed blender. Its penicillin content is satisfactory if it contains not less than 85 percent of the number of units that it is represented to contain.

(2) *Novobiocin content.* Use a suitable aliquot of the stock solution prepared as directed in paragraph (a)(1) of this section and proceed as directed in § 440.180d(b)(1)(ii) of this chapter. Its content of novobiocin is satisfactory if it contains not less than 85 percent of the number of milligrams that it is represented to contain.

(3) *Tetracycline phosphate complex content.* Proceed as directed in § 436.515(a)(1) of this chapter. Its potency is satisfactory if it contains the equivalent of not less than 85 percent of the number of milligrams of tetracycline hydrochloride that it is represented to contain.

(4) *Nystatin content.* Proceed as directed in § 446.181b(b)(1)(i)(b) of this chapter. Its nystatin content is satisfactory if it contains not less than 85 percent of the number of units that it is represented to contain.

(b) *Moisture.* Proceed as directed in § 440.80a(b)(5)(i) of this chapter.

§ 536.511 Penicillin-streptomycin-bacitracin methylene disalicylate-neomycin ointment; penicillin-dihydrostreptomycin-bacitracin methylene disalicylate-neomycin ointment.

The requirements for certification and the tests and methods of assay for penicillin-streptomycin-bacitracin methylene disalicylate-neomycin ointment; penicillin-dihydrostreptomycin-bacitracin methylene disalicylate-neomycin ointment are described under § 436.511 of this chapter.

§ 536.512 Procaine penicillin G-novobiocin-neomycin-dihydrostreptomycin in oil.

The requirements for certification and the tests and methods of assay for procaine penicillin G-novobiocin-neomycin-dihydrostreptomycin in oil are described under § 436.512 of this chapter.

§ 536.513 Streptomycin/dihydrostreptomycin for inhalation therapy.

(a) *Potency*—(1) *Streptomycin content*. Proceed as directed in § 444.70a(b)(1) of this chapter, except if it is packaged with inert gases proceed as follows: Use not less than 6 immediate containers. Place one-half the number of such containers in a suitable sharp freezing unit having a temperature not higher than -30°C . After freezing, cut open the containers and transfer the contents of each to a suitable beaker and allow gas to evaporate. After gas has evaporated, wash and dry the residue remaining in the container into the beaker with sterile distilled water, after which wash the entire contents of the beaker into a 500-milliliter volumetric flask and make to mark with sterile distilled water. Use an appropriate aliquot of each of these solutions and proceed as directed in § 444.70a(b)(1) of this chapter to determine the average total quantity of streptomycin in each container. Expel the drug from each of the remaining containers as directed in its labeling. After all gas (with drug) has been expelled, cut open the containers and place each in a large beaker containing 500 milliliters of sterile distilled water. Let stand for not less than 15 minutes, with frequent agitation. Remove an aliquot

and proceed as directed in § 444.70a(b)(1) of this chapter, to determine the quantity of streptomycin that remains in each container. The quantity of streptomycin expelled is determined by subtracting the average amount of the residue found from the average total amount contained in the containers. Its potency is satisfactory if it contains not less than 90 percent, or 85 percent if it is packaged with inert gases, of the number of milligrams of streptomycin that it is represented to contain.

(2) *Dihydrostreptomycin content*. Proceed as directed in paragraph (a)(1) of this section, except use the dihydrostreptomycin working standard as a standard of comparison. Its potency is satisfactory if it contains not less than 90 percent, or 85 percent if it is packaged with inert gases, of the number of milligrams of dihydrostreptomycin that it is represented to contain.

(b) *Unless it is packaged with inert gases, histamine, moisture, pH, streptomycin content (if it is dihydrostreptomycin), crystallinity (if it is crystalline dihydrostreptomycin)*. Proceed as directed in §§ 444.10a(b)(2), 444.70a(b)(3), (5), and (6) of this chapter.

(c) *If it is packaged with inert gases, moisture*. Proceed as directed in § 436.500(c) of this chapter, but in lieu of the directions for preparing the sample in § 436.500(c)(3) of this chapter prepare the sample and calculate as follows: Freeze the container as described in paragraph (a) of this section. After freezing, open the container and remove a representative 10-milliliter aliquot. Place this sample in a dry titrating vessel, immediately add an excess of Karl Fischer reagent, and back-titrate with water-methanol solution until the endpoint is reached.

Percent moisture =

$$\frac{(V_1 - V_2) \times c}{100}$$

[40 FR 13882, Mar. 27, 1975, as amended at 50 FR 19921, May 13, 1985]

§ 536.514

§ 536.514 Streptomycin sulfate/dihydrostreptomycin sulfate oral powder.

(a) *Potency*—(1) *Total potency*. Using the dihydrostreptomycin working standard as the standard of comparison, proceed as directed in § 444.70a(b)(1)(x) of this chapter. Its total potency is satisfactory if it contains not less than 90 percent of the combined number of milligrams of streptomycin and dihydrostreptomycin that it is represented to contain.

(2) *Streptomycin content*. Proceed as directed in § 444.211b(b)(2) of this chapter. Its content of streptomycin is satisfactory if it contains not less than 45 percent and not more than 55 percent of the total potency as determined under paragraph (a)(1) of this section.

(b) *Moisture*. Using a 1-gram sample, proceed as directed in § 440.80a(b)(5)(i) of this chapter.

§ 536.515 Dihydrostreptomycin-neomycin-polymyxin aerosol solution.

(a) *Potency*. (1) Using a separate graduate for each container to be tested, eject the drug as directed in its labeling. Measure the volume of each dose until the total contents are expelled. Remove appropriate aliquots and proceed as follows:

(i) *Dihydrostreptomycin content*. Using the dihydrostreptomycin working standard as the standard of comparison, proceed as directed in § 444.70a(b)(1) (i) through (ix) of this chapter. Its content of dihydrostreptomycin is satisfactory if it contains not less than 85 percent of the number of milligrams that it is represented to contain.

(ii) *Neomycin content*. Its content of neomycin is satisfactory if it contains not less than 85 percent of the number of milligrams that it is represented to contain.

(iii) *Polymyxin content*. Its content of polymyxin is satisfactory if it contains not less than 85 percent of the number of units that it is represented to contain.

(b) *pH*. Using the undiluted solution, proceed as directed in § 440.80a(b)(5)(ii) of this chapter.

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§ 536.516 Chlortetracycline-neomycin-streptomycin/dihydrostreptomycin penicillin ointment; tetracycline hydrochloride-neomycin-streptomycin/dihydrostreptomycin penicillin ointment.

(a) *Potency*—(1) *Penicillin content*. Place an accurately weighed sample of approximately 1 gram in an extraction funnel prepared by fusing a ground-glass joint to the top of a medium-porosity sintered-glass filter funnel (30-millimeter diameter). Wash with five 10-milliliter portions of warm isooctane and draw off the ointment base under vacuum. Discard the isooctane washings. Wash the residue with three 10-milliliter portions of chloroform and draw off under vacuum, combine the extracts, and make to mark in a 250-milliliter volumetric flask with absolute alcohol. Make the proper estimated dilutions in 1-percent phosphate buffer, at pH 6.0, and proceed as directed in § 440.80a(b)(1) of this chapter. Its content of penicillin is satisfactory if it contains not less than 85 percent of the number of units per gram of ointment that it is represented to contain.

(2) *Chlortetracycline content*. Wash the residue in the funnel four times with 10-milliliter portions of 0.3 percent piperidine in acetone solution. Withdraw each washing under vacuum. Combine the four washings in a 100-milliliter volumetric flask and make it mark with 0.1 M monopotassium phosphate buffer, pH 4.5. The sample may also be prepared by placing a representative portion (usually 1.0 gram, accurately weighed) in a glass blending jar containing 199 milliliters of 0.01 N HCl and 1.0 milliliter of polysorbate 80. Using a high-speed blender, blend the mixture for 2 to 3 minutes and make proper estimated dilutions in 0.1 M monopotassium phosphate buffer, pH 4.5, adding sufficient penicillinase to inactivate the penicillin. Proceed as directed in § 446.10a(b)(1)(viii) of this chapter. Its content of chlortetracycline is satisfactory if it contains not less than 85 percent of the number of milligrams per gram that it is represented to contain.

(3) *Tetracycline hydrochloride content*. Prepare the sample as directed in

paragraph (a)(2) of this section and proceed as directed in § 446.81a(b) of this chapter. Its content of tetracycline hydrochloride is satisfactory if it contains not less than 85 percent of the number of milligrams per gram of ointment that it is represented to contain.

(4) *Neomycin content.* The residue remaining in the funnel after the extraction described in paragraph (a)(2) of this section contains the neomycin and streptomycin or dihydrostreptomycin. Wash this residue five times, using 10-milliliter aliquots of 0.1 M phosphate buffer, pH 8.0, drawing each washing off under vacuum. Combine the washings in a 100-milliliter volumetric flask and make to mark with 0.1 M phosphate buffer, pH 8.0. Using an aliquot of this aqueous solution, proceed as directed in § 436.105 of this chapter. The content of neomycin is satisfactory if it contains not less than 85 percent of the number of milligrams per gram of ointment that it is represented to contain.

(5) *Streptomycin content.* Using an aliquot of the aqueous solution prepared in paragraph (a)(4) of this section, proceed as directed in § 444.70a(b)(1) (i) through (ix) of this chapter. The content of streptomycin is satisfactory if it contains not less than 85 percent of the number of milligrams per gram of ointment that it is represented to contain.

(6) *Dihydrostreptomycin content.* Using an aliquot of the aqueous solution prepared in paragraph (a)(4) of this section, and the dihydrostreptomycin working standard as a standard of comparison, proceed as directed in § 444.70a(b)(1) (i) through (ix) of this chapter. The content of dihydrostreptomycin is satisfactory if it contains not less than 85 percent of the number of milligrams per gram of ointment that it is represented to contain.

(b) *Moisture.* Proceed as directed in § 540.380a(b)(2) of this chapter.

§ 536.517 Calcium chlortetracycline-neomycin sulfate mastitis suspension.

(a) *Potency.*—(1) *Chlortetracycline content.* Proceed as directed in § 446.10a(b)(1)(viii) of this chapter, except prepare the sample as follows: Discharge a dose of the product com-

pletely into a glass blending jar. Add sufficient 0.01 N hydrochloric acid to give a total volume of 500 milliliters. Using a high-speed blender, blend the mixture for 2 to 3 minutes. Dilute an aliquot with 0.1 M phosphate buffer, pH 4.5, to the proper prescribed reference concentration. The chlortetracycline content of a single dose is satisfactory if it is equivalent to not less than 90 percent and not more than 125 percent of the number of milligrams of chlortetracycline hydrochloride that it is represented to contain.

(2) *Neomycin content.* Proceed as directed in § 444.42a(b)(1)(i) of this chapter, except prepare the sample as follows: Discharge a dose of the product completely into a glass blending jar. Add sufficient 0.1 M potassium phosphate buffer, pH 8.0, to give a total of 500 milliliters. Using a high-speed blender, blend the mixture for 2 to 3 minutes. Dilute an aliquot with 0.1 M potassium phosphate buffer, pH 8.0, to the proper prescribed reference concentration. The neomycin content of a single dose is satisfactory if it is not less than 90 percent and not more than 125 percent of the number of milligrams of neomycin that it is represented to contain.

(b) *Moisture.* Proceed as directed in § 540.380a(b)(2) of this chapter.

PART 539—BULK ANTIBIOTIC DRUGS SUBJECT TO CERTIFICATION

Subpart A—Bulk Provisions for Penicillin Antibiotic Drugs for Animal Use

Sec.

539.3 Sterile amoxicillin trihydrate.

539.15 Sterile sodium cloxacillin.

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539.170 Streptomycin sulfate veterinary grade; dihydrostreptomycin sulfate veterinary grade; dihydrostreptomycin hydrochloride veterinary grade.

Subpart C—Bulk Provisions for Tetracycline Antibiotic Drugs for Animal Use

539.210 Chlortetracycline bulk provisions.

539.210a Chlortetracycline.

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539.210c Chlortetracycline hydrochloride.

§ 539.3

Sec.

Subpart D—Bulk Provisions for Peptide Antibiotics for Animal Use

539.310 Bacitracin methylene disalicylate bulk provisions.

539.310a Bacitracin methylene disalicylate.

539.310b Soluble bacitracin methylene disalicylate.

AUTHORITY: Secs. 507, 512, 59 Stat. 463 as amended, 82 Stat. 343-351 (21 U.S.C. 357, 360b); 21 CFR 5.10, 5.83.

SOURCE: 40 FR 13885, Mar. 27, 1975, unless otherwise noted.

Subpart A—Bulk Provisions for Penicillin Antibiotic Drugs for Animal Use

§ 539.3 Sterile amoxicillin trihydrate.

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality, and purity.* Amoxicillin trihydrate is the trihydrate form of D(-) α -amino-p-hydroxybenzyl penicillin. It is so purified and dried that:

(i) Its potency is not less than 900 micrograms and not more than 1,050 micrograms of amoxicillin per milligram on an anhydrous basis.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) [Reserved]

(v) Its moisture content is not less than 11.5 percent and not more than 14.5 percent.

(vi) Its pH in an aqueous solution containing 2 milligrams per milliliter is not less than 3.5 and not more than 6.0.

(vii) Its amoxicillin content is not less than 90 percent on an anhydrous basis.

(viii) The acid-base titration concordance is such that the difference between the percent amoxicillin content when determined by nonaqueous acid titration and by nonaqueous base titration is not more than 6. The potency acid titration concordance is such that the difference between potency value divided by 10 and the percent amoxicillin content of the sample determined by the nonaqueous acid titration is not more than 6. The potency-base titration concordance is such that the difference between the potency value divided by 10 and the percent amoxicillin content of the sample de-

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termined by the nonaqueous base titration is not more than 6.

(ix) It is crystalline.

(x) It gives a positive identity test for amoxicillin trihydrate.

(2) *Labeling.* In addition to the labeling requirements prescribed by § 432.5(b) of this chapter, this drug shall be labeled "amoxicillin".

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, sterility, pyrogens, moisture, pH, amoxicillin content, concordance, crystallinity, and identity.

(ii) Samples required:

(a) For all tests except sterility: 10 packages, each containing approximately 600 milligrams.

(b) For sterility testing: 20 packages, each containing approximately 600 milligrams.

(b) *Tests and methods of assay—(1) Potency.* Use any of the following methods; however, the results obtained from the iodometric assay shall be conclusive:

(i) *Microbiological agar diffusion assay.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed portion of the sample in sufficient sterile distilled water to give a stock solution containing 1.0 milligram of amoxicillin per milliliter (estimated). Further dilute an aliquot of the stock solution with 0.1 M potassium phosphate buffer, pH 8.0 (solution 3) to the reference concentration of 0.1 microgram of amoxicillin per milliliter (estimated).

(ii) *Iodometric assay.* Proceed as directed in § 436.204 of this chapter, except in paragraph (d) of that section, add 3 drops of 1.2N hydrochloric acid to both the sample and working standard solutions after the addition of 0.01N iodine solution.

(iii) *Hydroxylamine colorimetric assay.* Proceed as directed in § 436.205 of this chapter.

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter using the method described in paragraph (e)(2) of that section, except use medium C in lieu of medium A, medium F in lieu of medium E, and during the period of

incubation shake the tubes at least once daily.

(3) *Pyrogens*. Proceed as directed in § 436.32(f) of this chapter, using a solution containing 20 milligrams of amoxicillin per milliliter.

(4) [Reserved]

(5) *Moisture*. Proceed as directed in § 436.201 of this chapter.

(6) *pH*. Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 2 milligrams per milliliter.

(7) *Amoxicillin content*. Proceed as directed in § 436.213 of this chapter, using both the titration procedures described in paragraph (e) (1) and (2) of that section. Calculate the percent amoxicillin content as follows:

(i) *Acid titration*.

Percent amoxicillin content =

$$\frac{(A-B) \text{ (normality of lithium methoxide reagent) (385.4) (100)}}{(100)}$$

$$\frac{(\text{weight of sample in milligrams}) (100 - m)}{10}$$

where:

A=Milliliters of lithium methoxide reagent used in titrating the sample.

B=Milliliters of lithium methoxide reagent used in titrating the blank.

m=Percent moisture content of the sample.

Difference =

$$\frac{\text{Potency in micrograms per milligram}}{10} \quad \text{--- percent amoxicillin content}$$

(ii) *Base titration*.

Percent amoxicillin content =

$$\frac{(A-B) \text{ (normality of perchloric acid reagent) (365.4) (100)}}{(100)}$$

$$\frac{(\text{weight of sample in milligrams}) (100 - m)}{10}$$

where:

A=Milliliters of perchloric acid reagent used in titrating the sample.

B=Milliliters of perchloric acid reagent used in titrating the blank.

m=Percent moisture content of the sample.

Difference =

$$\frac{\text{Potency in micrograms per milligram}}{10} \quad \text{--- percent amoxicillin content}$$

(8) *Crystallinity*. Proceed as directed in § 436.203(a) of this chapter.

(9) *Identity*. Proceed as directed in § 436.211 of this chapter, using a 0.5 percent potassium bromide disc prepared as described in paragraph (b)(1) of that section.

(Secs. 507, 512(n), 701(f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371(f) and (g)))

[43 FR 38000, Aug. 25, 1978, as amended at 49 FR 3459, Jan. 27, 1984; 50 FR 19921, May 13, 1985]

§ 539.15 Sterile sodium cloxacillin.

(a) *Requirements for certification*—

(1) *Standards of identity, strength, quality, and purity*. Sterile sodium cloxacillin is the monohydrate sodium salt of 5-methyl-3-(o-chloropenyl)-4-isoxazoly penicillin. It is so purified and dried that:

(i) Its potency is not less than 825 micrograms of cloxacillin per milligram.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) [Reserved]

(v) Its moisture content is not less than 3 percent and not more than 5 percent.

(vi) Its pH in an aqueous solution containing 10 milligrams per milliliter is not less than 4.5 nor more than 7.5.

(vii) Its cloxacillin content is not less than 82.5 percent.

(viii) It passes the identity test.

(ix) It is crystalline.

(2) *Labeling*. It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples*. In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, sterility, pyrogens, moisture, pH, cloxacillin content, identity, and crystallinity.

(ii) Samples required:

(a) For all tests except sterility: 10 packages, each containing approximately 300 milligrams.

(b) For sterility tests: 20 packages, each containing approximately 300 milligrams.

(b) *Tests and methods of assay*—(1) *Potency*. Use of any of the following methods; however, the results obtained from the microbiological agar diffusion assay shall be conclusive.

(i) *Microbiological agar diffusion assay*. Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed portion of the sample in sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with solution 1 to the reference concentration of 5 micrograms of cloxacillin per milliliter (estimated).

(ii) *Iodometric assay*. Proceed as directed in § 436.204 of this chapter.

(iii) *Hydroxylamine colorimetric assay*. Proceed as directed in § 436.205 of this chapter.

(2) *Sterility*. Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Pyrogens*. Proceed as directed in § 436.32(b) of this chapter, using a solution containing 20 milligrams of cloxacillin per milliliter.

(4) [Reserved]

(5) *Moisture*. Proceed as directed in § 436.201 of this chapter.

(6) *pH*. Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 10 milligrams per milliliter.

(7) *Cloxacillin content*. Accurately weigh approximately 100 milligrams of the sample and dissolve in sufficient 5N sodium hydroxide to give a total volume of 25 milliliters. Place in a boiling water bath for 30 minutes. Cool. Acidify 1 milliliter of solution with 1 milliliter of dilute sulfuric acid (1 in 2). Add 8 milliliters of water. Extract with two 25-milliliter portions of ethyl ether. Combine the ether extractives and extract with 25-milliliter portions of 0.1N sodium hydroxide. Combine the alkaline extractives and dilute the 100 milliliters with carbon-dioxide-free

water. Treat a portion of the cloxacillin working standard in the same manner. Using a suitable spectrophotometer, determine the absorbance of the solutions in a 1-centimeter cell at the absorption peaks at 257 ± 3 nanometers and at 282 ± 3 nanometers compared with a reagent blank. Determine the percent cloxacillin in the sample by means of the following calculation:

Percent of cloxacillin =

$$\frac{A_1 \times \text{Weight of standard in milligrams} \times \text{Percent of cloxacillin in standard}}{A_2 \times \text{Weight of sample in milligrams}} \times 100$$

where:

A_1 = Difference in absorbance for the sample between 257 nanometers and 282 nanometers.

A_2 = Difference in absorbance for the cloxacillin working standard, similarly treated.

(8) *Identity*. Proceed as directed in § 436.211 of this chapter, using the 0.5 percent potassium bromide disc described in paragraph (b)(1) of that section.

(9) *Crystallinity*. Proceed as directed in § 436.203 of this chapter.

[42 FR 64342, Dec. 23, 1977, as amended at 50 FR 19921, May 13, 1985]

Subpart B—Bulk Provisions for Oligosaccharide Antibiotic Drugs for Animal Use

§ 539.170 Streptomycin sulfate veterinary grade; dihydrostreptomycin sulfate veterinary grade; dihydrostreptomycin hydrochloride veterinary grade.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Streptomycin sulfate veterinary grade is the sulfate salt of a kind of streptomycin or a mixture of two or more such salts. Dihydrostreptomycin sulfate veterinary grade and dihydrostreptomycin hydrochloride veterinary grade are the hydrogenated sulfate or hydrochloride salt of a kind of streptomycin or a mixture of two or more such salts. Each such drug may contain a suitable and harmless lubricant. Each such drug is so purified and dried that:

(i) Its potency is not less than 450 micrograms per milligram.

(ii) [Reserved]

(iii) Its loss on drying is not more than 14.0 percent.

(iv) Its pH in aqueous solution of 0.2 gram per milliliter is not less than 3.0 and not more than 7.0.

(v) If it is dihydrostreptomycin sulfate veterinary grade or dihydrostreptomycin hydrochloride veterinary grade, its content of streptomycin is not more than 5 percent when calculated as streptomycin base.

(2) **Packaging.** In all cases the immediate containers shall be tight containers as defined by the U. S. P. The composition of the immediate container shall be such as will not cause any change in the strength, quality, or purity of the contents beyond any limit therefor in applicable standards, except that minor changes so caused which are normal and unavoidable in good packaging, storage, and distribution practice shall be disregarded.

(3) **Labeling.** Each package shall bear on its outside wrapper or container and the immediate container:

(i) The batch mark.

(ii) The number of milligrams of streptomycin or dihydrostreptomycin per gram and the number of grams of the drug in the immediate container; and if the batch contains a lubricant, the name of such ingredient.

(iii) The statement "Expiration date _____", the blank being filled in with the date which is 36 months after the month during which the batch was certified, except that the blank may be filled in with the date that is 48 months or 60 months after the month during which the batch was certified if the person who requests certification has submitted to the Commissioner results of tests and assays showing that after having been stored for such period of time such drug as prepared by him complies with the standards prescribed by paragraph (a)(1) of this section.

(iv) The statement "For use only in the manufacture of nonsterile veterinary drugs".

(4) **Request for certification; samples.** (i) In addition to complying with the requirements of § 514.50 of this chapter, a person who requests certification of a batch shall submit with his request a statement showing the batch mark, the number of packages of each size in the batch, the number of milligrams of streptomycin or dihydrostreptomycin per gram, and the total number of grams of streptomycin or dihydrostreptomycin in each package. Such request shall be accompanied or followed by the results of tests and assays made by him on the batch for potency, loss on drying, pH, and streptomycin content, if dihydrostreptomycin.

(ii) Such person shall submit with his request an accurately representative sample of the batch, consisting of 6 packages each containing approximately 1.0 gram taken from a different part of such batch, and each shall be packaged in accordance with the requirements of paragraph (a)(2) of this section.

(b) **Tests and methods of assay—(1) Potency.** If it is streptomycin sulfate veterinary grade, proceed as directed in § 444.70a(b)(1) of this chapter. If it is dihydrostreptomycin sulfate veterinary grade or dihydrostreptomycin hydrochloride veterinary grade, proceed as directed in § 444.70a(b)(1) of this chapter, using the dihydrostreptomycin working standard as the standard of comparison.

(2) [Reserved]

(3) **Loss on drying.** Using a 1-gram sample, proceed as directed in § 436.200(b) of this chapter.

(4) **pH.** Proceed as directed in § 436.202 of this chapter.

(5) **Streptomycin content (if it is dihydrostreptomycin).** Proceed as directed in § 444.10a(b)(2) of this chapter.

[40 FR 13885, Mar. 27, 1975, as amended at 42 FR 21276, Apr. 26, 1977; 50 FR 19921, May 13, 1985]

Subpart C—Bulk Provisions for Tetracycline Antibiotic Drugs for Animal Use

§ 539.210 Chlorotetracycline bulk provisions.

§ 539.210a Chlorotetracycline.

(a) **Requirements for certification—**

(1) **Standards of identity, strength, quality, and purity.** Chlorotetracycline

is a golden-yellow crystalline powder with the chemical structure 7-chloro-4-dimethylamino-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacene-carboxamide. It is so purified and dried that:

(i) Its potency is equivalent to not less than 968 micrograms of chlortetracycline hydrochloride per milligram when calculated on an anhydrous basis.

(ii) [Reserved]

(iii) Its moisture content is not more than 5.0 percent.

(iv) Its pH in an aqueous solution containing 10 milligrams per milliliter is not less than 4.0 and not more than 7.0.

(v) Its absorptivity at 445 mμ is 107.2 ± 4.0 percent of the chlortetracycline hydrochloride working standard similarly treated and both calculated on the anhydrous basis.

(2) *Packaging.* In all cases the immediate containers shall be tight containers as defined by the U.S.P., and shall be of such composition as will not cause any change in the strength, quality, or purity of the contents beyond any limits therefor in applicable standards, except that minor changes so caused that are normal and unavoidable in good packaging, storage, and distribution practice shall be disregarded.

(3) *Labeling.* Each package of chlortetracycline shall bear on its outside wrapper or container and the immediate container, as hereinafter indicated, the following:

(i) The batch mark.

(ii) The number of micrograms of chlortetracycline hydrochloride equivalent per milligram and the total number of grams in the immediate container.

(iii) The statement "Expiration date _____", the blank being filled in with the date that is 12 months after the month during which it was certified.

(iv) The statement "For use only in the manufacture of nonsterile veterinary drugs".

(v) The statement "Caution: Federal law prohibits dispensing without prescription".

(4) *Request for certification, check tests and assays; samples.* (i) In addition to complying with the requirements of § 431.1 of this chapter, a person who requests certification of a batch shall submit with his request a statement showing the batch mark, the number of packages of each size in the batch and (unless it was previously submitted) the date on which the latest assay of the drug comprising the batch was completed. Such request shall be accompanied or followed by results of tests and assays made by him on the batch for potency, moisture, pH, crystallinity, and absorptivity.

(ii) Such person shall submit with his request an accurately representative sample of the batch consisting of 10 packages, each containing approximately 300 milligrams taken from a different part of such batch and each packaged in accordance with the requirements of paragraph (a)(2) of this section.

(iii) In connection with contemplated requests for certification of batches of another drug in the manufacture of which chlortetracycline is to be used, the manufacturer of the batch that is to be so used may request the Commissioner to make check tests and assays on a sample of such batch taken as prescribed by paragraph (a)(4)(ii) of this section. From the information required by paragraph (a)(4)(i) of this section may be omitted results of tests and assays not required for the batch when used in such other drug. The Commissioner shall report to such manufacturer the results of such check tests and assays as are so requested.

(b) *Tests and methods of assay—(1) Potency.* Proceed as directed in § 446.10a(b)(1) of this chapter.

(2) [Reserved]

(3) *Moisture.* Proceed as directed in § 436.20(e)(2) of this chapter.

(4) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 10 milligrams per milliliter.

(5) *Microscopical test for crystallinity.* Mount a few particles of the sample in mineral oil and examine by means of a polarizing microscope. The particles reveal the phenomena of

birefringence and extinction positions on revolving the microscope stage.

(6) *Absorptivity*—(i) *Reagents*—(a) *Hydrochloric acid*. 5*N* and 1*N* aqueous solutions.

(b) *Sodium bisulfite*. 10 grams per 100 milliliters of water. This reagent must be freshly prepared.

(c) *Buffer solution*, pH 7.5. 178 grams of anhydrous K_2HPO_4 and 22 grams of anhydrous KH_2PO_4 per liter of water. Filter the solution before using.

(d) *Stock standard solution*. Weigh exactly 100.0 milligrams of chlortetracycline hydrochloride working standard and transfer to a 100-milliliter volumetric flask. Dilute to mark with water and mix well. Store in refrigerator (5° C. to 8° C.) in an amber bottle. The solution is stable and may be used for 1 week.

(e) *Working standard solution*. Pipet 10.0 milliliters of the stock standard solution into a 100-milliliter volumetric flask. Dilute to mark with water and mix well. Each milliliter contains 0.1 milligram of chlortetracycline hydrochloride. (Prepare just before using.)

(ii) *Preparation of sample*. Weigh accurately about 100 milligrams of sample and transfer to a 1-liter volumetric flask with the aid of water. Add 10 milliliters of 1*N* hydrochloric acid and 100 milliliters of water. Mix until solution is complete. Make to mark with water and mix thoroughly.

(iii) *Procedure*. (a) Pipe two 10.0-milliliter portions of the final dilution of the sample into each of two 50-milliliter volumetric flask, referred to in paragraph (b)(6)(iii) of this section as sample and sample blank, respectively.

(b) Pipet two 10.0-milliliter portions of the working standard into each of two 50-milliliter volumetric flasks, referred to in paragraph (b)(6)(iii) of this section as standard and standard blank, respectively.

(c) To the sample and the standard add in this order: 12 milliliters of 5*N* hydrochloric acid; 15 milliliters of buffer solution, pH 7.5; and 2 milliliters of sodium bisulfite solution. Suspend in a boiling water bath for exactly 7 minutes, and swirl occasionally. It is essential that the water boils throughout the entire heating period.)

(d) To the sample blank and standard blank, add 15 milliliters of buffer solution, pH, 7.5, and 2 milliliters of sodium bisulfite solution. Suspend in a boiling water bath for 5 minutes with occasional swirling. After exactly 5 minutes has elapsed add 12 milliliters of 5*N* hydrochloric acid and heat for an additional 2 minutes.

(e) After the completion of the heat treatment, immediately cool all the flasks under tap water. Fill each flask to mark with water and mix well.

(f) Read the absorbances of the standard and sample against their respective blanks at a wavelength of 445 mμ in a suitable spectrophotometer.

(iv) *Calculation*.

(4445 sample) (0.02) (1000) (50) (100) (100)

(4445 standard) (sample wt. in mg) (10) (100—percent moisture in sample)

=percent of absorptivity compared to the chlortetracycline hydrochloride working standard

(Sec. 507, 59 Stat. 463 as amended (21 U.S.C. 357); sec. 572, 82 Stat. 343-351 (21 U.S.C. 360b))

[40 FR 13835, Mar. 27, 1975, as amended at 43 FR 11177, Mar. 17, 1978; 50 FR 19921, May 13, 1985]

§ 539.210b Chlortetracycline bisulfate.

(a) *Requirements for certification*—

(1) *Standards of identity, strength, quality, and purity*. Chlortetracycline bisulfate is the crystalline acid sulfate salt of chlortetracycline, containing butyl alcohol bound to or complexed with it. It is so purified and dried that:

(i) Its potency is equivalent to not less than 760 micrograms of chlortetracycline hydrochloride per milligram when corrected for the moisture and butyl alcohol content.

(ii) [Reserved]

(iii) Its moisture content is not more than 2.0 percent.

(iv) Its butyl alcohol content is not more than 15 percent.

(v) Its sulfate content is not less than 15 percent when corrected for moisture and butyl alcohol content.

(vi) Its absorptivity, when corrected for its moisture and butyl alcohol content, is 89 percent $\pm$ 6 percent of that of the chlortetracycline hydrochloride

working standard similarly treated and calculated on the anhydrous basis.

(2) *Packaging.* In all cases, the immediate containers shall be tight containers as defined by the U.S.P. The composition of the immediate container shall be such as will not cause any change in the strength, quality, or purity of the contents beyond any limit therefor in applicable standards, except that minor changes so caused that are normal and unavoidable in good packaging, storage, and distribution practice shall be disregarded.

(3) *Labeling.* Each package shall bear on its outside wrapper or container and the immediate container:

- (i) The batch mark.
- (ii) The number of milligrams of chlortetracycline hydrochloride equivalent per gram and the number of grams in the immediate container.
- (iii) The statement "Expiration date _____", the blank being filled in with the date that is 48 months after the month during which the batch was certified.
- (iv) The statement "For use only in the manufacture of nonsterile veterinary drugs".

(4) *Request for certification; samples.* (i) In addition to complying with the requirements of § 431.1 of this chapter, a person who requests certification of a batch shall submit with his request a statement showing the batch mark, the number of packages of each size in the batch, the number of milligrams of chlortetracycline hydrochloride equivalent per gram, and the total number of grams in each package. Such request shall be accompanied or followed by the results of tests and assays made by him on the batch for potency, moisture, butyl alcohol content, sulfate content, absorptivity, and crystallinity.

(ii) Such person shall submit with his request an accurately representative sample of the batch, consisting of 10 packages each containing approximately 0.5 gram taken from a different part of such batch, and each shall be packaged in accordance with the requirements of paragraph (a)(2) of this section.

(b) *Tests and methods of assay—(1) Potency.* Using a 3.0-gram sample, pro-

ceed as directed in § 446.10a(b)(1) of this chapter.

(2) [Reserved]

(3) *Moisture.* Proceed as directed in § 436.200 of this chapter.

(4) *Butyl alcohol content—(i) Ceric nitrate reagent.* Dissolve 20 grams of ceric ammonium nitrate $((\text{NH}_4)_2\text{Ce}(\text{NO}_3)_6 \cdot 2\text{H}_2\text{O})$ in 4 M HNO_3 and make up to 100 milliliters with 4 M HNO_3 .

(ii) *Sample.* Accurately weigh an amount of sample calculated to contain approximately 30 milligrams of butyl alcohol and transfer it to a 50-milliliter round-bottom distillation flask. Dissolve the sample in 25 milliliters of distilled water, add a small amount of antifoam agent, and connect to a condenser terminating in an adapter. The end of the adapter is inserted deep into a 25-milliliter graduated cylinder, which stands in an ice water bath. Distill slowly until 7 to 8 milliliters have collected. Warm the distillate to room temperature, transfer to a 10-milliliter volumetric flask, using not more than 1 milliliter of water to rinse out the graduate, and make up to 10 milliliters. Pipette 5 milliliters of this into a test tube, add 2 milliliters of the ceric nitrate reagent, and mix.

(iii) *Standard.* Prepare a standard made by diluting 3 milliliters of reagent grade *n*-butyl alcohol with about 800 milliliters of distilled water in a 1,000-milliliter volumetric flask, shaking until solution is complete, then diluting to the mark with water. Use 5 milliliters of this plus 2 milliliters of ceric nitrate reagent as the standard.

(iv) *Blank solution.* Prepare a blank made by mixing 5 milliliters of distilled water with 2 milliliters of the ceric nitrate reagent.

(v) *Procedure.* Use a suitable spectrophotometer and 1-centimeter cells. Adjust the instrument to zero absorbance with the blank solution. Immediately read the absorbancies of the sample and the standard at 475 millimicrons. Calculate the percent butyl alcohol as follows:

Percent butyl alcohol =

$$\frac{A \text{ sample} \times 0.003 \times 10 \times 0.81 \times 100}{A \text{ standard} \times 0.98 \times w}$$

$$A \text{ standard} \times 0.98 \times w$$

Where:

A sample is the absorbance of the sample at 475 millimicrons;

A standard is the absorbance of the butyl alcohol standard containing 0.003 milliliter/milliliter;

w is the weight of sample in grams;

0.81 is the density of butyl alcohol; and

The factor 0.98 corrects for incomplete recovery of butyl alcohol in the distillation step.

distilled water and mix thoroughly. Transfer a 10.0 milliliter aliquot of this solution to a 250-milliliter volumetric flask, dilute to mark with 0.1 *N* hydrochloric acid, and mix thoroughly. Determine the absorbance of the solution at 368 millimicrons compared with distilled water as a blank. Use a suitable spectrophotometer for the absorbance measurements.

Absorptivity (1%, 1 cm.) =

$$\frac{\text{Absorbance at } 368m_{\mu} \times 2,500 \times 10}{\text{Weight of sample in milligrams} \times (100 - M - B)}$$

$$\text{Weight of sample in milligrams} \times (100 - M - B)$$

Where:

M = percent moisture in the sample;

B = percent butyl alcohol in the sample.

(7) *Crystallinity*. Proceed as directed in § 436.203(a) of this chapter.

(Sec. 507, 59 Stat. 463 as amended (21 U.S.C. 357); sec. 572, 82 Stat. 347-351 (21 U.S.C. 360b))

[40 FR 13885, Mar. 27, 1975, as amended at 43 FR 11177, Mar. 17, 1978; 50 FR 19921, May 13, 1985]

§ 539.210c Chlortetracycline hydrochloride.

(a) *Requirements for certification*. The requirements for certification of chlortetracycline hydrochloride are described in § 446.10 of this chapter, except if it is intended for use solely in the manufacture of an animal drug for nonparenteral use its potency is not less than 820 micrograms per milligram.

(b) *Tests and methods of assay*. The tests and methods are of assay for chlortetracycline are described in § 440.10 of this chapter.

(Sec. 572, 82 Stat. 343-351 (21 U.S.C. 360b))

[43 FR 11177, Mar. 17, 1978]

Subpart D—Bulk Provisions for Peptide Antibiotics for Animal Use

§ 539.310 Bacitracin methylene disalicylate bulk provisions.

[44 FR 22054, Apr. 13, 1979]

$$\frac{\text{Weight BaSO}_4 \times 0.4115 \times 100}{\text{Weight of sample}} = \text{percent sulfate}$$

$$\text{Weight of sample}$$

= percent sulfate

(6) *Absorptivity*. Accurately weigh approximately 100 milligrams of the sample and place in a 100-milliliter volumetric flask. Dissolve the sample in approximately 40 milliliters of distilled water by mixing thoroughly. Dilute to exactly 100 milliliters with

§ 539.310a

§ 539.310a Bacitracin methylene disalicylate.

(a) *Requirements for certification—*
(1) *Standards of identity, strength, quality, and purity.* The drug is the methylene disalicylate salt of a kind of bacitracin. It is so purified and dried that:

(i) Its potency is not less than 14 units of bacitracin per milligram on an anhydrous basis.

(ii) [Reserved]

(iii) Its loss on drying is not more than 7 percent.

(iv) Its pH is not less than 3.5 and not more than 5.0.

(2) *Labeling.* Each package shall bear on the outside wrapper or container and the immediate container:

(i) The batch mark.

(ii) The number of units of bacitracin per gram, the number of grams of bacitracin activity per pound, and the weight of the drug in the immediate container.

(iii) An expiration date prescribed for the drug as provided in § 432.5(a)(3) of this chapter.

(iv) The statement "For use only in the manufacture of nonsterile animal drugs".

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, loss on drying, and pH.

(ii) Samples required: 5 packages, each containing approximately 5 grams.

(b) *Tests and methods of assay—*(1) *Potency.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place an accurately weighed representative portion of the sample into a high-speed glass blender jar. Add 99 milliliters of 2 percent sodium bicarbonate solution (solution 14) and 1 milliliter of polysorbate 80. Blend for 3 minutes. Allow the foam to subside. Remove an aliquot of the solution and dilute with 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to the reference concentration of 1.0 unit of bacitracin per milliliter (estimated). At the reference concentration, the sample must

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have the same acidity as the standard, adding 0.01N HCl as needed.

(2) [Reserved]

(3) *Loss on drying.* Proceed as directed in § 436.200(b) of this chapter.

(4) *pH.* Proceed as directed in § 436.202 of this chapter, using a saturated solution (approximately 50 milligrams of the sample per milliliter).

[44 FR 22054, Apr. 13, 1979, as amended at 50 FR 19921, May 13, 1985]

§ 539.310b Soluble bacitracin methylene disalicylate.

(a) *Requirements for certification—*
(1) *Standards of identity, strength, quality, and purity.* The drug is the methylene disalicylate salt of a kind of bacitracin which has been solubilized with sodium bicarbonate. It is so purified and dried that:

(i) Its potency is not less than 8 units of bacitracin per milligram on an anhydrous basis.

(ii) [Reserved]

(iii) Its loss on drying is not more than 8.5 percent.

(iv) Its pH is not less than 8.0 and not more than 9.5.

(2) *Labeling.* Each package shall bear on the outside wrapper or container and the immediate container:

(i) The batch mark.

(ii) The number of units of bacitracin per gram, the number of grams of bacitracin activity per pound, and the weight of the drug in the immediate container.

(iii) An expiration date prescribed for the drug as provided in § 432.5(a)(3) of this chapter.

(iv) The statement "For use only in the manufacture of nonsterile animal drugs".

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, loss on drying, and pH.

(ii) Samples required: 5 packages, each containing approximately 5 grams.

(b) *Tests and methods of assay—*(1) *Potency.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place

an accurately weighed representative portion of the sample into a high-speed glass blender jar. Add 99 milliliters of 2 percent sodium bicarbonate solution (solution 14) and 1 milliliter of polysorbate 80. Blend for 3 minutes. Allow the foam to subside. Remove an aliquot of the solution and dilute with 1 percent potassium phosphate buffer, pH 6.0, (solution 1) to the reference concentration of 1.0 unit of bacitracin per milliliter (estimated). At the reference concentration, the sample must have the same acidity as the standard, adding 0.01N HCl as needed.

(2) [Reserved]

(3) *Loss on drying.* Proceed as directed in § 436.200(b) of this chapter.

(4) *pH.* Proceed as directed in § 436.202 of this chapter, using a solution containing approximately 25 milligrams of the sample per milliliter.

[44 FR 22054, Apr. 13, 1979, as amended at 50 FR 19921, May 13, 1985]

PART 540—PENICILLIN ANTIBIOTIC DRUGS FOR ANIMAL USE

Subpart A—Oral Dosage Forms

- Sec.
- 540.103 Amoxicillin oral dosage forms.
- 540.103a Amoxicillin trihydrate film-coated tablets.
- 540.103b Amoxicillin trihydrate for oral suspension.
- 540.103c Amoxicillin trihydrate oral suspension.
- 540.103d Amoxicillin trihydrate soluble powder.
- 540.103e Amoxicillin trihydrate boluses.
- 540.103f Amoxicillin trihydrate tablets.
- 540.103g Amoxicillin trihydrate and clavulanate potassium film-coated tablets.
- 540.103h Amoxicillin trihydrate and clavulanate potassium for oral suspension.
- 540.105 Ampicillin capsules.
- 540.107 Ampicillin trihydrate oral dosage forms.
- 540.107a Ampicillin trihydrate tablets.
- 540.107b Ampicillin trihydrate capsules.
- 540.107c Ampicillin trihydrate for oral suspension.
- 540.107d Ampicillin trihydrate soluble powder.
- 540.107e Ampicillin trihydrate boluses.
- 540.114 Benzathine cloxacillin.
- 540.114a Sterile benzathine cloxacillin.
- 540.119 Sodium dicloxacillin monohydrate capsules.

- Sec.
- 540.129 Potassium hetacillin oral dosage forms.
- 540.129a Potassium hetacillin tablets.
- 540.129b Potassium hetacillin capsules.
- 540.129c Potassium hetacillin oral suspension.
- 540.160 Dibenzylamine penicillin and potassium penicillin powder, buffered.
- 540.173 Potassium phenoxymethyl penicillin oral dosage forms.
- 540.173a Phenoxymethyl penicillin for oral suspension; potassium phenoxymethyl penicillin for oral solution.
- 540.173b Potassium phenoxymethyl penicillin tablets.
- 540.174 Procaine penicillin oral dosage forms.
- 540.174a Buffered penicillin powder, penicillin powder with buffered aqueous diluent.
- 540.181 Crystalline penicillin oral dosage forms.
- 540.181a [Reserved]
- 540.181b Potassium penicillin G in drinking water.

Subpart B—Implantation or Injectable Dosage Forms

- 540.203 Sterile amoxicillin trihydrate for suspension.
- 540.207 Sterile ampicillin trihydrate implantation and injectable dosage forms.
- 540.207a Sterile ampicillin trihydrate suspension.
- 540.207b Sterile ampicillin trihydrate for suspension.
- 540.209 Ampicillin sodium for aqueous injection.
- 540.255 Benzathine penicillin G implantation and injectable dosage forms.
- 540.255a Sterile benzathine penicillin G suspension.
- 540.255b [Reserved]
- 540.255c Sterile benzathine penicillin G and procaine penicillin G suspension.
- 540.261 Diethylaminoethyl ester penicillin G hydriodide for aqueous injection (penicillin G diethylaminoethyl ester hydriodide for aqueous injection).
- 540.274 Procaine penicillin G implantation and injectable dosage forms.
- 540.274a Procaine penicillin for aqueous injection.
- 540.274b Procaine penicillin G aqueous suspension.
- 540.274c Procaine penicillin G in oil.
- 540.274d Procaine penicillin in streptomycin sulfate solution; procaine penicillin in dihydrostreptomycin sulfate solution.
- 540.281 Crystalline penicillin implantation and injectable dosage forms.
- 540.281a [Reserved]
- 540.281b Buffered crystalline penicillin.

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Subpart C—Ophthalmic and Topical Dosage Forms

- 540.380 Penicillin ophthalmic and topical dosage forms.
540.380a Penicillin ointment.
540.380b Procaine penicillin-neomycin-polymyxin in oil; procaine penicillin-neomycin-polymyxin ointment.

Subparts D-E—[Reserved]

Subpart F—Intrauterine Dosage Forms

- 540.680 Ticarcillin.

Subpart G—[Reserved]

Subpart H—Intramammary Dosage Forms

- 540.803 Amoxicillin trihydrate for intramammary infusion.
540.814 Benzathine cloxacillin for intramammary infusion.
540.814a Sterile benzathine cloxacillin for intramammary infusion.
540.815 Sterile sodium cloxacillin for intramammary infusion.
540.815a Cloxacillin sodium for intramammary infusion.
540.829 Potassium hetacillin for intramammary infusion.
540.874 Procaine penicillin G intramammary dosage forms.
540.874a Procaine penicillin G in oil.
540.874b—540.874c [Reserved]
540.874d Penicillin G procaine-dihydrostreptomycin in soybean oil for intramammary infusion (dry cows).
540.874e Penicillin G procaine-dihydrostreptomycin sulfate for intramammary infusion (dry cows).
540.874f Procaine penicillin G-novobiocin for intramammary infusion.

AUTHORITY: Sec. 512, 82 Stat. 343-351 (21 U.S.C. 360b); 21 CFR 5.10 and 5.83.

SOURCE: 40 FR 13888, Mar. 27, 1975, unless otherwise noted.

Subpart A—Oral Dosage Forms

§ 540.103 Amoxicillin oral dosage forms.

[41 FR 5083, Feb. 4, 1976]

§ 540.103a Amoxicillin trihydrate film-coated tablets.

(a) *Requirements for certification—*
(1) *Standards of identity, strength, quality, and purity.* Amoxicillin trihydrate film-coated tablets are film-coated tablets composed of amoxicillin trihydrate with one or more suitable

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and harmless lubricants, diluents, binders, and colorings. Each tablet contains amoxicillin trihydrate equivalent to 50, 100, 150, 200 or 400 milligrams of amoxicillin. Its potency is satisfactory if it contains not less than 90 percent and not more than 120 percent of the amount of amoxicillin than it is represented to contain. The moisture content is not more than 7 percent. Tablets shall disintegrate within 30 minutes. They pass the identification test. The amoxicillin trihydrate used conforms to the requirements of § 440.3(a)(1) of this chapter.

(2) *Labeling.* It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter; in addition, this drug shall be labeled "amoxicillin tablets".

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each request shall contain:

(i) Results of tests and assays on:

(a) The amoxicillin trihydrate used in making the batch for potency, moisture, pH, amoxicillin content, concordance, crystallinity, and identity.

(b) The batch for potency, moisture, disintegration time, and identity.

(ii) Sample required for:

(a) The amoxicillin trihydrate used in making the batch: 12 packages, each containing approximately 30 milligrams.

(b) The batch: A minimum of 30 tablets.

(b) *Tests and methods of assay—*
Potency. Assay for potency by either of the following methods; however, the results obtained from the iodometric assay shall be conclusive:

(i) *Microbiological agar diffusion assay.* Proceed as directed in § 436.1 of this chapter, preparing the sample for assay as follows: Place a representative number of tablets into a high speed glass blender jar containing sufficient 0.1M potassium phosphate buffer, pH 8.0 (solution 3), to give stock solution of convenient concentration. Blend for 3 to 5 minutes. Remove an aliquot and further dilute with solution 3 to the reference concentration of approximately 0.1 microgram of amoxicillin per milliliter.

(ii) *Iodometric assay.* Proceed as directed in § 436.204 of this chapter, except in paragraph (d) of that section, add 3 drops of 1.2*N* hydrochloric acid to both the sample and working standard solutions after the addition of 0.01*N* iodine solution. Prepare the sample as follows: Place the contents of a representative number of tablets into a high-speed glass blender jar. Add sufficient distilled water to make a stock solution of convenient concentration. Blend for 3 to 5 minutes. Further dilute an aliquot with distilled water to the prescribed concentration.

(2) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(3) *Disintegration time.* Proceed as directed in § 436.212 of this chapter, using the procedure described in paragraph (e)(1) of that section.

(4) *Identity.* Proceed as directed in § 436.311 of this chapter, preparing the sample solution as follows: Dissolve an accurately weighed portion of the amoxicillin tablet contents in 0.1*N* hydrochloric acid to give a solution containing 4 milligrams of amoxicillin per milliliter.

(c) *Conditions of marketing—(1) Specifications.* The drug conforms to the requirements of paragraph (a) of this section.

(2) *Sponsor.* No. 000029 in § 510.600(c) of this chapter.

(3) *Conditions of use—(i) Dogs—(a) Amount:* 5 milligrams per pound of body weight, twice a day.

(b) *Indications for use.* It is used for the treatment of infections of the respiratory tract (tonsillitis, tracheobronchitis), genitourinary tract (cystitis), gastrointestinal tract (bacterial gastroenteritis), and soft tissues (abscesses, lacerations, wounds), caused by susceptible strains of *Staphylococcus aureus*, *Streptococcus* spp., *Escherichia coli*, *Proteus mirabilis*, and bacterial dermatitis caused by *Staphylococcus aureus*, *Streptococcus* spp., and *Proteus mirabilis*.

(c) *Limitations.* Administer for 5 to 7 days or 48 hours after all symptoms have subsided. If no improvement is seen in 5 days, review diagnosis and change therapy. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(ii) *Cats—(a) Amount:* 50 milligrams (5 to 10 milligrams per pound of body weight) once a day.

(b) *Indications for use.* It is used in the treatment of infections caused by susceptible organisms as follows: upper respiratory tract due to *Staphylococcus aureus*, *Streptococcus* spp., and *Escherichia coli*; genitourinary tract (cystitis) due to *Staphylococcus aureus*, *Streptococcus* spp., *Escherichia coli*, and *Proteus mirabilis*; gastrointestinal tract due to *Escherichia coli*; and skin and soft tissue (abscesses, lacerations, and wounds) due to *Staphylococcus aureus*, *Streptococcus* spp., *Escherichia coli*, and *Pasteurella multocida*.

(c) *Limitations.* Administer for 5 to 7 days or 48 hours after all symptoms have subsided. If no improvement is seen in 5 days, review diagnosis and change therapy. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(Secs. 507, 512(n), 701(f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371(f) and (g)))

[41 FR 5093, Feb. 4, 1976, as amended at 42 FR 49454, Sept. 27, 1977; 43 FR 24011, June 2, 1978; 49 FR 3459, Jan. 27, 1984; 50 FR 19922, May 13, 1985; 50 FR 24616, June 12, 1985]

§ 540.103b Amoxicillin trihydrate for oral suspension.

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality, and purity.* Amoxicillin trihydrate for oral suspension is a mixture of amoxicillin trihydrate with one or more suitable and harmless colorings, flavorings, buffers, sweetening ingredients, preservatives, stabilizers, and suspending agents. When reconstituted as directed in the labeling, it contains amoxicillin trihydrate equivalent to 50 milligrams of amoxicillin per milliliter. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the amount of amoxicillin that it is represented to contain. Its moisture content is not more than 3.0 percent. Its pH, when reconstituted as directed in the labeling, is not less than 5.0 and not more than 7.5. It passes the identity test. The amoxicillin trihydrate used con-

forms to the standards prescribed by § 440.3(a)(1) of this chapter.

(2) *Labeling.* It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter; in addition, this drug shall be labeled "amoxicillin for oral suspension."

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The amoxicillin trihydrate used in making the batch for potency, moisture, pH, amoxicillin content, concordance, crystallinity, and identity.

(b) The batch for potency, moisture, and identity.

(ii) Samples required:

(a) The amoxicillin trihydrate used in making the batch: 12 packages, each containing approximately 300 milligrams.

(b) The batch: A minimum of six immediate containers.

(b) *Tests and methods of assay—(1) Potency.* Assay for potency by either of the following methods; however, the results obtained from the iodometric assay shall be conclusive:

(i) *Microbiological agar diffusion assay.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Reconstitute the drug as directed in the labeling. Place an accurately measured representative portion of the sample into a suitable volumetric flask and dilute to volume with 0.1M potassium phosphate buffer, pH 8.0 (solution 3), to give a stock solution of convenient concentration. Mix well. Further dilute an aliquot with solution 3 to the reference concentration of 0.1 microgram of amoxicillin per milliliter (estimated).

(ii) *Iodometric assay.* Proceed as directed in § 436.204 of this chapter, except in paragraph (d) of that section, add 3 drops of 1.2N hydrochloric acid to both the sample and working standard solutions after the addition of 0.01N iodine solution. Prepare the sample as follows: Reconstitute the drug as directed in the labeling. Place an accurately measured aliquot (usually a single dose) in a suitable volumetric flask. Dilute to volume with distilled water. Mix well. Further dilute

with distilled water to the prescribed concentration.

(2) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(3) *pH.* Proceed as directed in § 436.202 of this chapter, using the suspension reconstituted as directed in the labeling.

(4) *Identity.* Proceed as directed in § 436.311 of this chapter, preparing the sample solution as follows: Place a 2-gram weighed portion of the sample into a 50-milliliter volumetric flask. Dilute to volume with 0.1N hydrochloric acid and shake for 5 minutes.

(c) *Conditions of marketing—(1) Specifications.* The drug conforms to the requirements for certification as in paragraph (a) of this section.

(2) *Conditions of use—(1) Sponsor.* See No. 000029 in § 510.600(c) of this chapter.

(a) *Dogs—(1) Dosage.* 5 milligrams per pound of body weight twice daily.

(2) *Indications for use.* For the treatment of infections caused by susceptible strains of organisms as follows: respiratory tract (tonsillitis, tracheobronchitis) caused by *Staphylococcus aureus*, *Streptococcus* spp., *Escherichia coli*, and *Proteus mirabilis*; genitourinary tract (cystitis) caused by *Staphylococcus aureus*, *Streptococcus* spp., *Escherichia coli*, and *Proteus mirabilis*; gastrointestinal tract (bacterial gastroenteritis) caused by *Staphylococcus aureus*, *Streptococcus* spp., *Escherichia coli*, and *Proteus mirabilis*; bacterial dermatitis caused by *Staphylococcus aureus*, *Streptococcus* spp. and *Proteus mirabilis*; and soft tissues (abscesses, lacerations, and wounds) caused by *Staphylococcus aureus*, *Streptococcus* spp., *Escherichia coli*, and *Proteus mirabilis*.

(b) *Cats—(1) Dosage.* 50 milligrams (5 to 10 milligrams per pound) once daily.

(2) *Indications for use.* For the treatment of infections caused by susceptible strains of organisms as follows: upper respiratory tract due to *Staphylococcus* spp., *Streptococcus* spp., *Hemophilus* spp., *Escherichia coli*, *Pasteurella* spp., and *Proteus mirabilis*; genitourinary tract (cystitis) due to *Staphylococcus aureus*, *Streptococcus* spp., *Escherichia coli*, *Proteus mirabilis*, and *Corynebacterium* spp.

gastrointestinal tract due to *Escherichia coli*, *Proteus* spp., *Staphylococcus* spp., and *Streptococcus* spp., skin and soft tissue (abscesses, lacerations, and wounds) due to *Staphylococcus* spp., *Streptococcus* spp., *Escherichia coli*, and *Pasteurella multocida*.

(c) *Limitations*. Use for 5 to 7 days or 48 hours after all symptoms have subsided. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(ii) *Sponsor*. See Nos. 000031 and 000332 in § 510.600(c) of this chapter.

(a) *Dogs*—(1) *Dosage*. 5 milligrams per pound of body weight twice daily.

(2) *Indications for use*. For the treatment of bacterial dermatitis due to *Staphylococcus aureus*, *Streptococcus* spp., *Staphylococcus* spp., and *Escherichia coli*, and soft tissue infections (abscesses, wounds, lacerations) due to *Staphylococcus aureus*, *Streptococcus* spp., *Escherichia coli*, *Proteus mirabilis* and *Staphylococcus* spp.

(b) *Limitations*. Use for 5 to 7 days. Continue for 48 hours after all symptoms have subsided. If no improvement is seen in 5 days, review diagnosis and change therapy. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(Secs. 507, 512(n), 701(f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371(f) and (g)))

[42 FR 5350, Jan. 28, 1977, as amended at 48 FR 41579, Sept. 16, 1983; 49 FR 3459, Jan. 27, 1984; 50 FR 19922, May 13, 1985]

§ 540.103c Amoxicillin trihydrate oral suspension.

(a) *Requirements for certification*—

(1) *Standards of identity, strength, quality, and purity*. Amoxicillin trihydrate oral suspension is composed of amoxicillin trihydrate with a suitable and harmless preservative and gelling agent suspended in soybean oil base. The drug is packaged in a multiple-dose container incorporating a suitable dosing pump. Each 0.8-milliliter dose contains amoxicillin trihydrate equivalent to 40 milligrams of amoxicillin. Its potency is satisfactory if it is not less than 90 percent of the labeled amount of amoxicillin. Its moisture content is not more than 2 percent. It passes the identity test for amoxicillin. The

amoxicillin trihydrate used conforms to the standards prescribed by § 440.3(a)(1) of this chapter.

(2) *Labeling*. It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter. In addition, it shall be labeled "amoxicillin oral suspension."

(3) *Request for certification; samples*. In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) The results of tests and assays on:

(a) The amoxicillin trihydrate used in making the batch for potency, moisture, pH, amoxicillin content, concordance, crystallinity, and identity.

(b) The batch for potency, moisture, and identity.

(ii) *Samples required*:

(a) The amoxicillin trihydrate used in making the batch: 12 packages, each containing approximately 300 milligrams.

(b) The batch: A minimum of eight immediate containers.

(b) *Tests and methods of assay*—(1) *Potency*. Assay for potency by either of the following methods; however, the results obtained from the microbiological assay shall be conclusive:

(i) *Microbiological agar diffusion assay*. Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Using the dosing pump, deliver one dose of the sample into a high-speed glass blender jar containing 1 milliliter of polysorbate 80 and sufficient 0.1 M potassium phosphate buffer, pH 8.0 (solution 3) to give a final volume of 500 milliliters. Blend for 3 to 5 minutes. Further dilute an aliquot of this stock solution with solution 3 to the reference concentration of 0.1 microgram of amoxicillin per milliliter (estimated).

(ii) *Iodometric assay*. Proceed as directed in § 436.204 of this chapter, except in paragraph (d) of that section, add 3 drops of 1.2N hydrochloric acid to both the sample and working standard solutions after the addition of 0.01N iodine solution. Prepare the sample as follows: Place an accurately measured aliquot (usually 5 pump doses) in a separatory funnel containing 100 milliliters of petroleum ether. Shake vigorously until homogeneous.

Add 140 milliliters of distilled water. Shake for 5 minutes. Allow the layers to separate. Drain the lower aqueous layer into a 250-milliliter volumetric flask. Repeat the extraction twice with 50-milliliter portions of distilled water. Combine the second and third extractives with the first. Dilute to volume with distilled water.

(2) *Moisture*. Proceed as directed in § 436.201 of this chapter.

(3) *Amoxicillin identity*. Proceed as directed in § 436.311 of this chapter preparing the sample solution as follows: Place 1.0 milliliter of the well shaken sample into a 50-milliliter volumetric flask. Bring to volume with a 4:1 solution of acetone and 0.1 N hydrochloric acid.

(c) *Conditions of marketing—(1) Specifications*. The drug conforms to the requirements of paragraph (a) of this section.

(2) *Sponsor*. See No. 000029 in § 510.600(c) of this chapter.

(3) *Related tolerances*. See § 556.510 of this chapter.

(4) *Conditions of use in swine—(i) Amount*. 40 milligrams orally twice a day using a dosing pump.

(ii) *Indications for use*. For the treatment of baby pigs under 10 pounds for porcine colibacillosis caused by *Escherichia coli* susceptible to amoxicillin.

(iii) *Limitations*. Treat animals for 48 hours after all symptoms have subsided but not beyond 5 days. Do not slaughter during treatment or for 15 days after latest treatment. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(Secs. 507, 512(n), 701(f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371(f) and (g)))

[43 FR 4601, Feb. 3, 1978, as amended at 43 FR 16312, Apr. 18, 1978; 49 FR 3460, Jan. 27, 1984; 50 FR 19922, May 13, 1985]

§ 540.103d Amoxicillin trihydrate soluble powder.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity*. Amoxicillin trihydrate soluble powder is a dry mixture of amoxicillin trihydrate with one or more suitable and harmless diluents and stabilizing agents. Each gram con-

tains an amount of amoxicillin trihydrate equivalent to 115.4 milligrams of amoxicillin. Its potency is satisfactory if it contains not less than 90 percent and not more than 120 percent of the number of milligrams of amoxicillin it is represented to contain. Its moisture content is not more than 5.0 percent. Its pH in an aqueous solution containing 2 milligrams of amoxicillin per milliliter is not less than 3.5 and not more than 6.0. The amoxicillin trihydrate used conforms to the standards prescribed by § 440.3(a)(1) of this chapter.

(2) *Labeling*. It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter. In addition, this drug shall be labeled "amoxicillin soluble powder, veterinary."

(3) *Requests for certification; samples*. In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The amoxicillin trihydrate used in making the batch for potency, moisture, pH, amoxicillin content, concordance, crystallinity, and identity.

(b) The batch for potency, moisture, and pH.

(ii) *Samples required*:

(a) The amoxicillin trihydrate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch: A minimum of five immediate containers.

(b) *Tests and methods of assay—(1) Potency*. Assay for potency by either of the following methods; however, the results obtained from the iodometric assay shall be conclusive:

(i) *Microbiological agar diffusion assay*. Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample, usually 1 gram, in sufficient 0.1M potassium phosphate buffer, pH 8.0 (solution 3) to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with solution 3 to the reference concentration of 0.1 microgram of amoxicillin per milliliter (estimated).

(ii) *Iodometric assay*. Proceed as directed in § 436.204 of this chapter, preparing the sample as follows: Dissolve

An accurately weighed sample, usually 1 gram, in sufficient distilled water to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with distilled water to the prescribed concentration.

(2) *Moisture*. Proceed as directed in § 436.201 of this chapter.

(3) *pH*. Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 20 milligrams of amoxicillin per milliliter.

(c) *Conditions of marketing*—(1) *Specifications*. The drug conforms to the requirements of paragraph (a) of this section.

(2) *Sponsor*. See No. 000029 in § 510.600(c) of this chapter.

(3) *Related tolerances*. See § 556.38 of this chapter.

(4) *Conditions of use in non-ruminating calves*—(i) *Amount*. 400 milligrams per 100 pounds of body weight twice daily.

(ii) *Indications for use*. For the treatment of bacterial enteritis when due to susceptible *Escherichia coli* in non-ruminating calves.

(iii) *Limitations*. Administer by drench or by mixing in milk. Treatment should be continued for 48 hours after all symptoms have subsided but not to exceed 5 days. For use in non-ruminating calves only, not for use in other animals which are raised for food production. Do not slaughter animals during treatment or for 20 days after the latest treatment. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[47 FR 35758, Aug. 17, 1982, as amended at 50 FR 19922, May 13, 1985]

§ 540.103e Amoxicillin trihydrate boluses.

(a) *Requirements for certification*—

(1) *Standards of identity, strength, quality, and purity*. Amoxicillin trihydrate boluses are composed of amoxicillin trihydrate with or without one or more suitable and harmless diluents, fillers, binder-disintegrators, pigments, and lubricants. Each bolus contains the equivalent of 400 milligrams of amoxicillin. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the amount of amoxicillin that it is represented to contain. The mois-

ture content is not more than 7.5 percent. The amoxicillin trihydrate used conforms to the requirements of § 440.3(a)(1) of this chapter.

(2) *Labeling*. It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter, and in addition, this drug shall be labeled "amoxicillin boluses, veterinary."

(3) *Requests for certification; samples*. In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of test and assays on:

(a) The amoxicillin trihydrate used in making the batch for potency, moisture, pH, amoxicillin content, concordance, crystallinity, and identity.

(b) The batch for potency and moisture.

(ii) Samples required.

(a) The amoxicillin trihydrate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch: A minimum of 36 boluses.

(b) *Tests and methods of assay*—(1) *Potency*. Assay for potency by either of the following methods; however, the results obtained from the iodometric assay shall be conclusive:

(i) *Microbiological agar diffusion assay*. Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place a representative number of boluses into a high-speed blender jar containing sufficient 0.1M potassium phosphate buffer, pH 8.0 (solution 3), to give a stock solution of convenient concentration. Blend for 3 to 5 minutes. Remove an aliquot and further dilute with solution 3 to the reference concentration of approximately 0.1 microgram of amoxicillin per milliliter.

(ii) *Iodometric assay*. Proceed as directed in § 436.204 of this chapter, preparing the sample as follows: Place a representative number of boluses in a high-speed glass blender jar and add sufficient distilled water to give a convenient concentration. Blend for 3 to 5 minutes. Further dilute an aliquot with distilled water to the prescribed concentration.

(2) *Moisture*. Proceed as directed in § 436.201 of this chapter.

(c) *Conditions of marketing*—(1) *Specifications*. The drug conforms to the requirements of paragraph (a) of this section.

(2) *Sponsor*. See No. 000029 in § 510.600(c) of this chapter.

(3) *Related tolerances*. See § 556.38 of this chapter.

(4) *Conditions of use in non-ruminating calves*—(i) *Amount*. 400 milligrams per 100 pounds of body weight twice daily.

(ii) *Indications for use*. For the treatment of bacterial enteritis when due to susceptible *Escherichia coli* in non-ruminating calves.

(iii) *Limitations*. For oral use in non-ruminating calves only, not for use in other animals which are raised for food production. Treatment should be continued for 48 hours after all symptoms have subsided but not to exceed 5 days. Do not slaughter animals during treatment or for 20 days after the latest treatment. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[47 FR 35757, Aug. 17, 1982, as amended at 50 FR 19922, May 13, 1985]

§ 540.103f Amoxicillin trihydrate tablets.

(a) *Requirements for certification*—

(1) *Standards of identity, strength, quality, and purity*. Amoxicillin trihydrate tablets are composed of amoxicillin trihydrate with or without one or more suitable and harmless lubricants, fillers, binder-disintegrants, and buffers. Each tablet contains amoxicillin trihydrate equivalent to 50, 100, 200, or 400 milligrams of amoxicillin. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the amount of amoxicillin that it is represented to contain. The moisture content is not more than 6 percent. Tablets disintegrate within 30 minutes. It passes the identity test. The amoxicillin trihydrate used conforms to the requirements of § 440.3(a)(1) of this chapter.

(2) *Labeling*. It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter, and in addition, this drug shall be labeled "amoxicillin tablets."

(3) *Requests for certification; samples*. In addition to complying with the

requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The amoxicillin trihydrate used in making the batch for potency, moisture, pH, amoxicillin content, concordance, crystallinity, and identity.

(b) The batch for potency, moisture, disintegration time, and identity.

(ii) *Samples required*.

(a) The amoxicillin trihydrate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch: A minimum of 36 tablets.

(b) *Tests and methods of assay*—(1) *Potency*. Assay for potency by either of the following methods; however, the results obtained from the iodometric assay shall be conclusive:

(i) *Microbiological agar diffusion assay*. Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place a representative number of tablets into a high-speed blender jar containing sufficient 0.1M potassium phosphate buffer, pH 8.0 (solution 3), to give a stock solution of convenient concentration. Blend for 3 to 5 minutes. Remove an aliquot and further dilute with solution 3 to the reference concentration of 0.1 microgram of amoxicillin per milliliter (estimated).

(ii) *Iodometric assay*. Proceed as directed in § 436.204 of this chapter, preparing the sample as follows: Place a representative number of tablets in a high-speed glass blender jar and add sufficient distilled water to give a convenient concentration. Blend for 3 to 5 minutes. Further dilute an aliquot with distilled water to the prescribed concentration.

(2) *Moisture*. Proceed as directed in § 436.201 of this chapter.

(3) *Disintegration time*. Proceed as directed in § 436.212 of this chapter, using the procedure described in paragraph (e)(1) of that section.

(4) *Identity*. Proceed as directed in § 436.311 of this chapter, preparing the sample as follows: Using a mortar and pestle, grind a representative number of tablets into a fine powder. Dissolve an accurately weighed amount of this powder in 0.1N hydrochloric acid to give a solution contain-

ing 4 milligrams of amoxicillin per milliliter.

(c) *Conditions of marketing*—(1) *Specifications*. The drug conforms to the requirements of paragraph (a) of this section.

(2) *Sponsor*. See 000031 or 000332 in § 510.600(c) of this chapter.

(3) *Conditions of use*—(i) *Dogs*—(a) *Dosage*: 5 milligrams per pound of body weight twice a day.

(b) *Indications for use*: Treatment of bacterial dermatitis due to *Staphylococcus aureus*, *Streptococcus* spp., *Staphylococcus* supp., and *E. coli*; and soft tissue infections (abscesses, wounds, lacerations) due to *Staphylococcus aureus*, *Streptococcus* spp., *E. coli*, *Proteus mirabilis*, and *Staphylococcus* spp.

(c) *Limitations*. Use for 5 to 7 days or 48 hours after all symptoms have subsided. If no improvement is seen in 5 days, review diagnosis and change therapy. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(ii) [Reserved]

[48 FR 20901, May 10, 1983, as amended at 48 FR 33864, July 26, 1983; 50 FR 19922, May 13, 1985]

§ 540.103g Amoxicillin trihydrate and clavulanate potassium film-coated tablets.

(a) *Requirements for certification*—

(1) *Standards of identity, strength, quality, and purity*. Amoxicillin trihydrate and clavulanate potassium tablets are film-coated tablets composed of amoxicillin trihydrate and clavulanate potassium with or without one or more suitable and harmless lubricants, diluents, and binders. Each tablet contains amoxicillin trihydrate and clavulanic acid as the potassium salt equivalent to either 50 milligrams of amoxicillin and 12.5 milligrams clavulanic acid, or 100 milligrams of amoxicillin and 25 milligrams clavulanic acid, or 200 milligrams amoxicillin and 50 milligrams clavulanic acid or 300 milligrams amoxicillin and 75 milligrams clavulanic acid. Its amoxicillin trihydrate content is satisfactory if it contains not less than 90 percent and not more than 120 percent of the number of milligrams of amoxicillin that it is represented to contain. Its clavulanate potassium content is satisfactory if it

contains not less than 90 percent and not more than 120 percent of the number of milligrams of clavulanic acid that it is represented to contain. Its moisture content is not more than 10 percent. Tablets shall disintegrate within 30 minutes. The amoxicillin trihydrate conforms to the standards prescribed by § 440.3(a)(1) of this chapter. The clavulanate potassium conforms to the standards prescribed by § 455.15(a)(1) of this chapter.

(2) *Labeling*. It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter; in addition, this drug shall be labeled "amoxicillin and clavulanate potassium tablets".

(3) *Requests for certification; samples*. In addition to complying with the requirements of § 431.1 of this chapter, each request shall contain:

(i) Results of tests and assays on:

(a) The amoxicillin trihydrate used in making the batch for potency, moisture, pH, amoxicillin content, concordance, crystallinity, and identity.

(b) The clavulanate potassium used in making the batch for clavulanic acid content, moisture, pH, identity, and clavam-2-carboxylate content.

(c) The batch for amoxicillin contents, clavulanic acid content, moisture, and disintegration time.

(ii) *Sample required for*:

(a) The amoxicillin trihydrate used in making the batch: 12 packages, each containing approximately 300 milligrams.

(b) The clavulanate potassium used in making the batch: 12 packages, each containing approximately 300 milligrams.

(c) The batch: A minimum of 100 tablets.

(b) *Tests and methods of assay*—(1) *Amoxicillin and clavulanic acid contents*. Proceed as in § 440.103d(b) of this chapter.

(2) *Moisture*. Proceed as directed in § 436.201 of this chapter.

(3) *Disintegration time*. Proceed as directed in § 436.212 of this chapter, using the procedure described in paragraph (e)(1) of that section.

(c) *Conditions of marketing*—(1) *Specifications*. The drug conforms to the requirements of paragraph (a) of this section.

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(2) *Sponsor.* See No. 000029 in § 510.600(c) of this chapter.

(3) *Conditions of use—(i) Dogs—(a) Amount.* 6.25 milligrams per pound of body weight twice daily (equivalent to 5 milligrams amoxicillin and 1.25 milligrams clavulanic acid per pound body weight).

(b) *Indications for use.* It is used for treatment of skin and soft tissue infections such as wounds, abscesses, cellulitis, superficial/juvenile and deep pyoderma due to susceptible strains of beta-lactamase (penicillinase) producing *Staphylococcus aureus*, non-beta-lactamase *Staphylococcus aureus*, *Staphylococcus* spp., *Streptococcus* spp., and *E. coli*.

(c) *Limitations.* Wounds, abscesses, cellulitis, and superficial/juvenile pyoderma: Treat for 5 to 7 days or for 48 hours after all signs have subsided. If no improvement is seen after 5 days of treatment, discontinue therapy and reevaluate the case. Deep pyoderma may require treatment for 21 days; do not treat for more than 30 days. Not for use in dogs maintained for breeding. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(ii) *Cats—(a) Amount.* 62.5 milligrams twice daily (50 milligrams amoxicillin and 12.5 milligrams clavulanic acid).

(b) *Indications for use.* It is used in the treatment of skin and soft tissue infections such as wounds, abscesses and cellulitis/dermatitis due to susceptible strains of beta-lactamase (penicillinase) producing *Staphylococcus aureus*, non-beta-lactamase producing *Staphylococcus aureus*, *Staphylococcus* spp., *Streptococcus* spp., *E. coli*, and *Pasteurella* spp. It is also used in the treatment of urinary tract infections (cystitis) due to susceptible strains of *E. coli*.

(c) *Limitations.* Skin and soft tissue infections: abscesses, cellulitis/dermatitis should be treated for 5 to 7 days or for 48 hours after all signs have subsided. If no response is seen after 3 days of treatment, therapy should be discontinued and the case reevaluated. Urinary tract infections may require treatment for 10 to 14 days or longer. The maximum duration of treatment should not exceed 30 days. Safety of

use in pregnant or breeding animals has not been established. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[49 FR 45421, Nov. 16, 1984; 49 FR 48271, Dec. 12, 1984, as amended at 50 FR 19922, May 13, 1985; 51 FR 4484, Feb. 5, 1986; 51 FR 5318, Feb. 13, 1986; 53 FR 235, Jan. 6, 1988]

§ 540.103h Amoxicillin trihydrate and clavulanate potassium for oral suspension.

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality, and purity.* Amoxicillin trihydrate and clavulanate potassium for oral suspension is a dry mixture of amoxicillin trihydrate and clavulanate potassium with one of more suitable and harmless flavorings, sweetening ingredients, stabilizers, and suspending agents. When reconstituted as directed in the labeling, each milliliter contains amoxicillin trihydrate equivalent to 50 milligrams of amoxicillin with clavulanate potassium equivalent to 12.5 milligrams of clavulanic acid. Its amoxicillin trihydrate content is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of amoxicillin that it is represented to contain. Its clavulanate potassium content is satisfactory if it is not less than 90 percent and not more than 125 percent of the number of milligrams of clavulanic acid that it is represented to contain. The moisture content of the dry powder is not more than 8.5 percent. When reconstituted as directed in the labeling, its pH is not less than 4.8 and not more than 6.6. The amoxicillin trihydrate conforms to the standards prescribed by § 440.3(a)(1) of this chapter. The clavulanate potassium conforms to the standards prescribed by § 455.15(a)(1) of this chapter.

(2) *Labeling.* The drug shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter; in addition, it shall be labeled "amoxicillin and clavulanate potassium for oral suspension, veterinary".

(3) *Requests for certification; samples.* In addition to complying with the

requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:
(a) The amoxicillin trihydrate used in making the batch for potency, moisture, pH, amoxicillin content, concordance, crystallinity, and identity.

(b) The clavulanate potassium used in making the batch for clavulanic acid content, moisture, pH, identity, and clavam-2-carboxylate content.

(c) The batch for amoxicillin content, clavulanic acid content, moisture, and pH.

(ii) Samples required:

(a) The amoxicillin trihydrate used in making the batch: 12 packages, each containing approximately 300 milligrams.

(b) The clavulanate potassium used in making the batch: 12 packages, each containing approximately 300 milligrams.

(c) The batch: A minimum of 6 immediate containers.

(b) Tests and methods of assay—(1) Amoxicillin and clavulanic acid contents. Proceed as in § 440.103e(b) of this chapter.

(2) Moisture. Proceed as in § 436.201 of this chapter.

(3) pH. Proceed as in § 436.202 of this chapter, using the suspension reconstituted as directed in the labeling.

(c) Conditions of marketing—(1) Specifications. The drug conforms to the requirements of paragraph (a) of this section.

(2) Sponsor. See 000029 in § 510.600(c) of this chapter.

(3) Conditions of use—(i) Dogs—(a) Amount. 6.25 milligrams per pound of body weight twice daily (equivalent to 5 milligrams amoxicillin and 1.25 milligrams clavulanic acid per pound body weight).

(b) Indications for use. For the treatment of skin and soft tissue infections such as wounds, abscesses, cellulitis, superficial/juvenile and deep pyoderma due to susceptible strains of beta-lactamase (penicillinase) producing *Staphylococcus aureus*, non-beta-lactamase *Staphylococcus aureus*, *Staphylococcus* spp., *Streptococcus* spp., and *E. coli*.

(c) Limitations. Administer for 5 to 7 days or 48 hours after all symptoms have subsided. Deep pyoderma may re-

quire 21 days, not to exceed 30 days. If no improvement is seen in 5 days, discontinue therapy and reevaluate the case. Not for use in dogs maintained for breeding. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(ii) Cats—(a) Amount. 62.5 milligrams (1 milliliter) twice daily (50 milligrams of amoxicillin and 12.5 milligrams clavulanic acid).

(b) Indications for use. It is used in the treatment of feline skin and soft tissue infections such as wounds, abscesses, and cellulitis/dermatitis due to susceptible strains of beta-lactamase (penicillinase) producing *Staphylococcus aureus*, non-beta-lactamase *Staphylococcus aureus*, *Staphylococcus* spp., *Streptococcus* spp., *E. coli*, *Pasteurella multocida*, and *Pasteurella* spp.

(c) Limitations. Administer 48 hours after all symptoms have subsided. If no improvement is seen after 3 days of treatment, discontinue therapy and reevaluate the case. Maximum duration of treatment should not exceed 30 days. Not for use in cats maintained for breeding. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[51 FR 4483, Feb. 5, 1986, as amended at 51 FR 5317, Feb. 13, 1986; 51 FR 6218, Feb. 21, 1986]

§ 540.105 Ampicillin capsules.

(a) Requirements for certification—

(1) Standards of identity, strength, quality, and purity. Ampicillin capsules are composed of ampicillin with or without one or more buffer substances, diluents, binders, lubricants, vegetable oils, colorings, and flavorings, enclosed in a gelatin capsule. Each capsule contains 125 milligrams or 250 milligrams of ampicillin. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of ampicillin that it is represented to contain. The loss on drying is not more than 4.0 percent. The ampicillin used conforms to the standards prescribed by § 440.5(a)(1) of this chapter.

(2) Labeling. It shall be labeled in accordance with the requirements of

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paragraph (c) of this section and § 510.55 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The ampicillin used in making the batch for potency, loss on drying, pH, ampicillin content, concordance, crystallinity, and identity.

(b) The batch for potency and loss on drying.

(ii) Samples required:

(a) The ampicillin used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch: A minimum of 30 capsules.

(b) *Tests and methods of assay*—(1) *Potency.* Assay for potency by either of the following methods; however, the results obtained from the microbiological agar diffusion assay shall be conclusive.

(i) *Microbiological agar diffusion assay.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place a representative number of capsules into a high-speed glass blender jar with sufficient 0.1M potassium phosphate buffer, pH 8.0 (solution 3), to give a convenient concentration. Blend for 3 to 5 minutes. Remove an aliquot and further dilute with solution 3 to the reference concentration of 0.1 microgram of ampicillin per milliliter (estimated).

(ii) *Iodometric assay.* Proceed as directed in § 436.204 of this chapter, except in paragraph (d) of that section, add 3 drops of 1.2N hydrochloric acid to both the sample and working standard solutions after the addition of 0.01N iodine solution. Prepare the sample as follows: Place the contents of a representative number of capsules into a high-speed glass blender jar. Add sufficient distilled water to give a stock solution of convenient concentration. Blend 3 to 5 minutes. Filter through Whatman No. 2 filter paper. Further dilute an aliquot of the filtrate with distilled water to the prescribed concentration.

(2) *Loss on drying.* Proceed as directed in § 436.200(a) of this chapter.

(c) *Conditions of marketing*—(1) *Specifications.* The drug conforms to

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the certification requirements of paragraph (a) of this section.

(2) *Sponsor.* See No. 000008 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) The drug is administered orally as follows:

(a) To dogs:

(1) In the treatment of urinary tract infections (cystitis) due to *Proteus spp.*, hemolytic and non-hemolytic streptococci, beta hemolytic streptococci and *E. coli*.

(2) In upper respiratory tract infections tracheobronchitis (kennel cough), tonsillitis due to alpha and beta hemolytic streptococci, hemolytic positive *Staphylococci*, *E. coli* and *Proteus spp.*

(3) In infections associated with abscesses, lacerations, and wounds due to *Staphylococcus spp.* and *Streptococcus spp.*

(b) To cats:

(1) In respiratory tract infections (bacterial pneumonia) due to alpha and beta hemolytic streptococci, hemolytic positive *staphylococci*, *E. coli*, and *Proteus spp.*

(2) In infections associated with abscesses, lacerations, and wounds due to *Staphylococcus spp.* and *Streptococcus spp.*

(ii) Dosage is recommended as follows:

(a) In dogs 5 to 10 milligrams per pound of body weight, e.g., one 125 milligram capsule per 14 to 25 pounds, given 2 to 4 times daily; for those weighing 6 to 14 pounds, one capsule twice daily is suggested.

(b) In cats, 125 milligrams twice daily; in more acute conditions three times daily.

(iii) Bacteriologic studies to determine the causative organisms and their susceptibility to ampicillin should be performed.

(iv) Use of the drug is contraindicated in animals with a history of an allergic reaction to any of the penicillins. Ampicillin is contraindicated in infections caused by penicillinase-producing organisms.

(v) Not for use in animals which are raised for food production.

(vi) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(Secs. 507, 512(n), 701(f) and (g), 52 Stat. 1053-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371(f) and (g)))

[40 FR 13888, Mar. 27, 1975, as amended at 49 FR 3460, Jan. 27, 1984; 50 FR 19922, May 13, 1985]

§ 540.107 Ampicillin trihydrate oral dosage forms.

§ 540.107a Ampicillin trihydrate tablets.

(a) Requirements for certification—

(1) *Standards of identity, strength, quality, and purity.* Ampicillin trihydrate tablets are composed of ampicillin trihydrate with suitable binders, fillers, lubricants, expanders, coloring, and flavoring. Each tablet contains 50 or 100 milligrams of ampicillin. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of ampicillin that it is represented to contain. Its loss on drying is not more than 10 percent. The tablets disintegrate within 30 minutes. The ampicillin trihydrate used conforms to the standards prescribed by § 440.7 of this chapter. Each other ingredient used, if its name is recognized in the U.S.P. or N.F., conforms to the standards prescribed therefor by such official compendium.

(2) *Packaging.* It shall be packaged in accordance with the requirements of § 510.45 of this chapter.

(3) *Labeling.* It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter, and shall, in addition, be labeled "veterinary ampicillin tablets".

(4) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The ampicillin trihydrate used in making the batch for potency, moisture, pH, ampicillin content, concordance, crystallinity, and identity.

(b) The batch for potency, loss on drying, and disintegration time.

(ii) Samples required:

(a) The ampicillin trihydrate used in making the batch: 10 containers, each containing not less than 300 milligrams.

(b) The batch: A minimum of 36 tablets.

(b) *Tests and methods of assay—(1) Potency.* Use either of the following methods; however, the results obtained from the microbiological agar diffusion assay shall be conclusive:

(i) *Microbiological agar diffusion assay.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place a representative number of tablets into a high-speed glass blender jar with sufficient 0.1 M potassium phosphate buffer, pH 8.0 (solution 3), to give a stock solution of convenient concentration. Blend for 3 to 5 minutes. Further dilute an aliquot of the stock solution with solution 3 to the reference concentration of 0.1 microgram of ampicillin per milliliter (estimated).

(ii) *Iodometric assay.* Proceed as directed in § 436.204 of this chapter, except in paragraph (d) of that section, add 3 drops of 1.2N hydrochloric acid to both the sample and working standard solutions after the addition of 0.01N iodine solution. Prepare the sample as follows: Place a representative number of tablets into a high-speed glass blender jar. Add sufficient distilled water to give a stock solution of convenient concentration. Blend for 3 minutes. Further dilute an aliquot of the stock solution with distilled water to give the prescribed concentration.

(2) *Loss on drying.* Proceed as directed in § 436.200(a) of this chapter.

(3) *Disintegration time.* Proceed as directed in § 436.212 of this chapter using the procedure described in paragraph (e)(1) of that section.

(c) *Conditions of marketing—(1) Specifications.* The drug contains ampicillin as ampicillin trihydrate and conforms to the certification requirements of paragraph (a) of this section.

(2) *Sponsor.* See No. 000029 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) Dogs: The drug is administered orally for the treatment of infections caused by susceptible organisms as follows:

(a) Respiratory tract infections: Upper respiratory infections, tonsillitis, and bronchitis due to *Streptococcus spp.*, *Staphylococcus spp.*, *Escherichia coli*, *Proteus mirabilis*, and *Pasteurella spp.*

(b) Urinary tract infections (cystitis) due to *Streptococcus* spp., *Staphylococcus* spp., *Escherichia coli*, *Proteus mirabilis*, and *Enterococcus* spp.

(c) Gastrointestinal infections due to *Staphylococcus* spp., *Streptococcus* spp., *Enterococcus* spp., and *Escherichia coli*.

(d) For the treatment of infections associated with abscesses, lacerations, and wounds caused by *Staphylococcus* spp., and *Streptococcus* spp.

(ii) Dosage of 5 mg per pound of body weight, at 8-hour intervals, 1 to 2 hours prior to feeding, to be continued 36 to 48 hours after all symptoms have subsided. If no improvement is seen within 5 days, stop treatment, reevaluate diagnosis, and change therapy.

(iii) It is not for use in animals which have shown hypersensitivity to penicillin or for infections caused by penicillinase-producing organisms.

(iv) It is not for use in animals which are raised for food production.

(v) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(Secs. 507, 512(n), 701(f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371(f) and (g)))

(40 FR 13888, Mar. 27, 1975, as amended at 41 FR 18652, May 6, 1976; 45 FR 48129, July 18, 1980; 49 FR 3460, Jan. 27, 1984; 50 FR 19922, May 13, 1985)

§ 540.107b Ampicillin trihydrate capsules.

(a) *Requirements for certification*—

(1) *Standards of identity, strength, quality, and purity.* Ampicillin trihydrate capsules are composed of ampicillin trihydrate with or without one or more diluents, binders, or lubricants, enclosed in a gelatin capsule. Each capsule contains ampicillin trihydrate equivalent to 125, 250, or 500 milligrams of ampicillin. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of ampicillin that it is represented to contain. Its loss on drying is not less than 10 percent and not more than 15 percent. The ampicillin trihydrate used conforms to the standards prescribed by § 440.7(a)(1) of this chapter.

(2) *Labeling.* It shall be labeled in accordance with the requirements of

paragraph (c) of this section and § 510.55 of this chapter, and, in addition, this drug shall be labeled "ampicillin capsules, veterinary."

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The ampicillin trihydrate used in making the batch for potency, loss on drying, pH, ampicillin content, concordance, crystallinity, and identity.

(b) The batch for potency and loss on drying.

(ii) Samples required:

(a) The ampicillin trihydrate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch: A minimum of 30 capsules.

(b) *Tests and methods of assay*—(1) *Potency.* Assay for potency by either of the following methods; however, the results obtained from the microbiological agar diffusion assay shall be conclusive.

(i) *Microbiological agar diffusion assay.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place a representative number of capsules into a high-speed glass blender jar with sufficient 0.1M potassium phosphate buffer, pH 8.0 (solution 3), to give a convenient concentration. Blend for 3 to 5 minutes. Remove an aliquot and further dilute with solution 3 to the reference concentration of 0.1 microgram of ampicillin per milliliter (estimated).

(ii) *Iodometric assay.* Proceed as directed in § 436.204 of this chapter, except in paragraph (d) of that section, add 3 drops of 1.2N hydrochloric acid to both the sample and working standard solutions after the addition of 0.01N iodine solution. Prepare the sample as follows: Place the contents of a representative number of capsules into a high-speed glass blender jar. Add sufficient distilled water to give a stock solution of convenient concentration. Blend for 3 minutes. Filter through Whatman No. 2 filter paper. Further dilute an aliquot of the filtrate with distilled water to the prescribed concentration.

(2) *Loss on drying.* Proceed as directed in § 436.200(a) of this chapter.

(c) *Conditions of marketing—(1) Specifications.* The drug is in capsule form and conforms to the certification requirements of paragraph (a) of this section.

(2) *Sponsor.* See No. 053501 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) It is used in dogs as follows:

(a) It is administered as a treatment against strains of gram-negative and gram-positive organisms sensitive to ampicillin and associated with respiratory tract infections (tracheobronchitis and tonsillitis); urinary tract infections (cystitis); bacterial gastroenteritis; generalized infections (septicemia) associated with abscesses, lacerations, and wounds; and bacterial dermatitis.

(b) Administer 5 to 10 milligrams per pound of body weight two or three times daily. In severe or acute conditions, 10 milligrams per pound of body weight should be given three times daily. Dosage should be administered 1 to 2 hours prior to feeding.

(ii) It is used in cats as follows:

(a) It is administered as a treatment against strains of gram-negative and gram-positive organisms sensitive to ampicillin and associated with respiratory tract infections (bacterial pneumonia); urinary tract infections (cystitis); and generalized infections (septicemia) associated with abscesses, lacerations, and wounds.

(b) Administer 10 to 30 milligrams per pound of body weight two or three times daily. Dosage should be administered 1 to 2 hours prior to feeding.

(iii) The drug may be given as an emergency measure; however, in vitro sensitivity tests on samples collected prior to treatment should be made. Ampicillin is contraindicated for use in infections caused by penicillinase-producing organisms and for use in dogs and cats known to be allergic to any of the penicillins. It is also not to be used in animals raised for food production.

(iv) For use only by or on the order of a licensed veterinarian.

[40 FR 13888, Mar. 27, 1975, as amended at 49 FR 3460, Jan. 27, 1984; 50 FR 19922, May 13, 1985; 50 FR 41490, Oct. 11, 1985]

§ 540.107c Ampicillin trihydrate for oral suspension.

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality, and purity.* Ampicillin trihydrate for oral suspension is a mixture of ampicillin trihydrate with one or more suitable and harmless colorings, flavorings, buffers, sweetening ingredients, and preservatives. When reconstituted as directed in the labeling, it contains ampicillin trihydrate equivalent to 25 milligrams of ampicillin per milliliter. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of ampicillin that it is represented to contain. Its moisture content is not more than 2.5 percent. Its pH, when reconstituted as directed in the labeling, is not less than 5.0 and is not more than 7.5. The ampicillin trihydrate used conforms to the standards prescribed by § 440.7(a)(1) of this chapter.

(2) *Labeling.* The drug shall be labeled in accordance with the requirements prescribed by paragraph (c) of this section and § 510.55 of this chapter, and in addition, it shall be labeled "ampicillin for oral suspension, veterinary".

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The ampicillin trihydrate used in making the batch for potency, loss on drying, pH, ampicillin content, concordance, crystallinity, and identity.

(b) The batch for potency, moisture, and pH.

(ii) Samples required:

(a) The ampicillin trihydrate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch: A minimum of six immediate containers.

(b) *Tests and methods of assay—(1) Potency.* Assay for potency by either of the following methods; however, the results obtained from the micro-

biological agar diffusion assay shall be conclusive:

(i) *Microbiological agar diffusion assay.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Reconstitute the drug as directed in the labeling. Place an accurately measured representative portion of the sample into a suitable volumetric flask and dilute to volume 0.1M potassium phosphate buffer, pH 8.0 (solution 3), to give a convenient concentration. Mix well. Further dilute an aliquot with solution 3 to the reference concentration of 0.1 microgram of ampicillin per milliliter (estimated).

(ii) *Iodometric assay.* Proceed as directed in § 436.204 of this chapter, except in paragraph (d) of that section, add 3 drops of 1.2N hydrochloric acid to both the sample and working standard solutions after the addition of 0.01N iodine solution. Prepare the sample as follows: Reconstitute the drug as directed in the labeling. Place an accurately measured aliquot, usually a single dose, in a suitable volumetric flask. Dilute to volume with distilled water. Mix well. Further dilute with distilled water to the prescribed concentration.

(2) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(3) *pH.* Proceed as directed in § 436.202 of this chapter, using the drug reconstituted as directed in the labeling.

(c) *Conditions of marketing—(1) Specifications.* The drug contains ampicillin as ampicillin trihydrate and conforms to the requirements of paragraph (a) of this section. When reconstituted as directed in the labeling, it contains 125 milligrams of ampicillin per 5 milliliters of suspension.

(2) *Sponsor.* See No. 053501 in § 510.600(c) of this chapter.

(3) *Conditions of use—(i) Dogs.* (a) It is indicated in the treatment of respiratory tract infections (tracheobronchitis and tonsillitis) due to *E. coli*, *Pseudomonas spp.*, *Proteus spp.*, *Staphylococcus spp.*, and *Streptococcus spp.*, urinary tract infections (cystitis) due to *E. coli*, *Staphylococcus spp.*, *Streptococcus spp.*, and *Proteus spp.*; bacterial gastroenteritis due to *E. coli*; generalized infections (septic-

mia) associated with abscesses, lacerations, and wounds, due to *Staphylococcus spp.* and *Streptococcus spp.*; bacterial dermatitis due to *Staphylococcus spp.*, *Streptococcus spp.*, *Proteus spp.* and *Pseudomonas spp.*

(b) It is administered orally, 5 to 10 milligrams per pound of body weight or 3 times daily, 1 to 2 hours prior to feeding. In severe or acute conditions 10 milligrams per pound of body weight 3 times daily.

(ii) *Cats.* (a) It is indicated in the treatment of respiratory tract infections (bacterial pneumonia) due to *Staphylococcus spp.*, *Streptococcus spp.*, *E. coli*, and *Proteus spp.*; urinary tract infections (cystitis) due to *E. coli*, *Staphylococcus spp.*, *Streptococcus spp.*, *Proteus spp.*, and *Corynebacterium spp.*; generalized infection (septicemia) associated with abscesses, lacerations, and wounds, due to *Staphylococcus spp.*, *Streptococcus spp.*, *Bacillus spp.*, and *Pasteurella spp.*

(b) It is administered orally, 10 to 20 milligrams per pound of body weight or 3 times daily, 1 to 2 hours prior to feeding.

(iii) *Duration of treatment.* In dogs and cats, duration of treatment is usually 3 to 5 days. Continue treatment 48 hours after the animal's temperature has returned to normal and all other signs of infection have subsided. If no response is obtained within 3 to 5 days, reevaluate diagnosis and treatment. Appropriate laboratory tests should be conducted, including in vitro culturing and susceptibility tests on samples collected prior to treatment.

(iv) *Restrictions.* Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(Secs. 507, 512(n), 701(f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 360b(n), 371(f) and (g)))

[40 FR 13888, Mar. 27, 1975, as amended at 49 FR 3460, Jan. 27, 1984; 50 FR 16922, Mar. 13, 1985; 50 FR 41490, Oct. 11, 1985]

§ 540.107d Ampicillin trihydrate soluble powder.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Ampicillin trihydrate soluble powder is a dry mixture

of ampicillin trihydrates with one or more suitable and harmless diluents and stabilizing agents. Each gram contains an amount of ampicillin trihydrate equivalent to 88.2 milligrams of ampicillin. Its potency is satisfactory if it contains not less than 90 percent and not more than 120 percent of the number of milligrams of ampicillin it is represented to contain. Its moisture content is not more than 5.0 percent. Its pH in an aqueous solution containing 20 milligrams of ampicillin per milliliter is not less than 3.5 and not more than 6.0. The ampicillin trihydrate used conforms to the standards prescribed by § 440.7(a)(1) of this chapter.

(2) *Labeling.* It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter, and in addition, this drug shall be labeled "ampicillin soluble powder, veterinary".

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The ampicillin trihydrate used in making the batch for potency, loss on drying, pH, ampicillin content, concordance, crystallinity, and identity.

(b) The batch for potency, moisture and pH.

(ii) Samples required:

(a) The ampicillin trihydrate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch: A minimum of five immediate containers.

(b) *Tests and methods of assay—(1) Potency.* Assay for potency by either of the following methods; however, the results obtained from the microbiological agar diffusion assay shall be conclusive:

(i) *Microbiological agar diffusion assay.* Proceed as directed in § 436.195 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample, usually 1 gram, in sufficient 0.1M potassium phosphate buffer, pH 8.0 (solution 3) to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with solution 3 to the reference concentration

of 0.1 microgram of ampicillin per milliliter (estimated).

(ii) *Iodometric assay.* Proceed as directed in § 436.204 of this chapter, except in paragraph (d) of that section, add 3 drops of 1.2N hydrochloric acid to both the sample and working standard solutions after the addition of 0.01N iodine solution. Prepare the sample as follows: Dissolve an accurately weighed sample, usually 1 gram, in sufficient distilled water to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with distilled water to the prescribed concentration.

(2) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(3) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 20 milligrams of ampicillin per milliliter.

(c) *Conditions of marketing—(1) Specifications.* The drug conforms to the certification requirements of paragraph (a) of this section.

(2) *Sponsor.* See No. 053501 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) Indicated for oral use in swine in the treatment of porcine colibacillosis (*E. coli*) and salmonellosis (*Salmonella spp.*) infections in swine up to 75 pounds of body weight, and bacterial pneumonia caused by *Pasteurella multocida*, *Staphylococcus spp.*, *Streptococcus spp.*, and *Salmonella spp.*

(ii) The drug is administered at a dosage level of 5 milligrams of ampicillin activity per pound of body weight twice daily, administered orally by gavage or in drinking water for up to 5 days.

(iii) For use in swine only. Not for use in other animals which are raised for food production. Treated swine must not be slaughtered for food during treatment and for 24 hours following the last treatment.

(iv) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(Secs. 507, 512(n), 701(f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371(f) and (g)))

[40 FR 13888, Mar. 27, 1975, as amended at 49 FR 3460, Jan. 27, 1984; 50 FR 19922, May 13, 1985; 50 FR 41490, Oct. 11, 1985]

§ 540.107e Ampicillin trihydrate boluses.

(e) *Requirements for certification—*

(1) *Standards of identity, strength, quality and purity.* Ampicillin trihydrate boluses are composed of ampicillin trihydrate with or without one or more suitable and harmless diluents, buffers, preservatives, stabilizing agents and lubricants. Each bolus contains the equivalent of 400 milligrams of ampicillin. Its potency is satisfactory if it is not less than 90 and not more than 120 percent of the number of milligrams of ampicillin that it is represented to contain. Its loss on drying is not more than 5 percent. The ampicillin trihydrate used conforms to the standards prescribed in § 440.7(a)(1) of this chapter.

(2) *Labeling.* It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter, and, in addition, this drug shall be labeled "ampicillin boluses, veterinary."

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The ampicillin trihydrate, used in making the batch, for potency, loss on drying, pH, ampicillin content, concordance, crystallinity, and identity.

(b) The batch for potency and loss on drying.

(ii) Samples required:

(a) The ampicillin trihydrate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch: A minimum of 36 boluses.

(b) *Test and methods of assay—(1) Potency.* Use either of the following methods, however, the results obtained from the microbiological agar diffusion assay shall be conclusive:

(i) *Microbiological agar diffusion assay.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place a representative number of boluses into a high-speed glass blending jar with sufficient 0.1M potassium phosphate buffer pH 8.0 (solution 3) to give a stock solution of convenient concentration. Blend for 3 to 5 minutes. Remove an aliquot and further dilute

with solution 3 to the reference concentration of 0.1 microgram ampicillin per milliliter (estimated).

(ii) *Iodometric assay.* Proceed as directed in § 436.204 of this chapter, except in paragraph (d) of that section, add 3 drops of 1.2N hydrochloric acid to both the sample and working standard solutions after the addition of 0.01N iodine solution. Prepare the sample as follows: Place a representative number of boluses into a high-speed glass blender jar. Add sufficient distilled water to give a stock solution of convenient concentration. Blend for 3 to 5 minutes. Further dilute an aliquot of the stock solution with distilled water to the prescribed concentration.

(2) *Loss on drying.* Proceed as directed in § 436.200(a) of this chapter.

(c) *Conditions of marketing—(1) Specifications.* The drug is in bolus form and conforms to the certification requirements of paragraph (a) of this section.

(2) *Related tolerances.* See § 556.40 of this chapter.

(3) *Labeling statements.* (i) For oral use in nonruminating calves only.

(ii) Not for use in other animals which are raised for food production.

(iii) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(4) *Conditions of use.* (i) *Sponsor.* See No. 053501 in § 510.600(c) of this chapter.

(a) It is administered orally to nonruminating calves for the treatment of colibacillosis caused by *E. coli*, bacterial enteritis caused by *Salmonella* spp., and bacterial pneumonia caused by *Pasteurella* spp.

(b) It is administered at a dosage level of 5 milligrams per pound of body weight twice daily for up to 5 days.

(c) Treated calves must not be slaughtered for food during treatment and for 15 days after the last treatment.

(ii) *Sponsor.* See No. 000029 in § 510.600(c) of this chapter.

(a) It is administered orally to nonruminating calves for the treatment of bacterial enteritis (colibacillosis) caused by *E. coli*.

(b) It is administered at a dosage level of 5 milligrams per pound of body weight twice daily. Treatment should not exceed 4 days.

(c) Treated calves must not be slaughtered for food during treatment and for 7 days after the last treatment.

(Secs. 507, 512(n), 701(f) and (g); 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371(f) and (g)))

[40 FR 13888, Mar. 27, 1975, as amended at 40 FR 55849, Dec. 2, 1975; 41 FR 30326, July 23, 1976; 49 FR 3460, Jan. 27, 1984; 50 FR 19922, May 13, 1985; 50 FR 41490, Oct. 11, 1985]

§ 540.114 Benzathine cloxacillin.

(a) Requirements for certification—

(1) *Standards of identity, strength, quality, and purity.* Benzathine cloxacillin is the *N,N'*-dibenzyleth-ylenediamine salt of 5-methyl-3-(*o*-chlorophenyl)-4-isoxazolyl penicillin. It is so purified and dried that:

(i) Its potency is not less than 704 nor more than 821 micrograms of cloxacillin per milligram on an anhydrous basis.

(ii) [Reserved]

(iii) Its moisture content is not more than 5.0 percent.

(iv) Its pH in an aqueous suspension containing 10 milligrams per milliliter is not less than 3.0 nor more than 6.5.

(v) It passes the identity test.

(vi) It is crystalline.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, moisture, pH, identity, and crystallinity.

(ii) Samples required: 10 packages, each containing approximately 300 milligrams.

(b) *Tests and methods of assay—(1) Potency.* Use the microbiological agar diffusion assay method. Proceed in accordance with § 436.105 of this chapter, using the cloxacillin working standard as the standard of comparison and preparing the sample for assay as follows: Dissolve an accurate-

ly weighted portion of the sample in sufficient methanol to give a convenient stock solution. Immediately dilute an aliquot of this stock solution with solution 1 to the reference concentration of 5 micrograms of cloxacillin per milliliter estimated.

(2) [Reserved]

(3) *Moisture.* Proceed in accordance with § 436.201 of this chapter.

(4) *pH.* Proceed in accordance with § 436.202 of this chapter, using an aqueous suspension prepared by adding 10 milligrams per milliliter.

(5) *Identity.* Transfer approximately 20 milligrams of the sample to a 50-milliliter Erlenmeyer flask. Add 5.0 milliliters of 5*N* sodium hydroxide and heat in a steam bath 20 minutes. Cool. Transfer 1 milliliter to an extraction funnel; add approximately 10 milliliters of water and 1 milliliter of dilute sulfuric acid (1:2). Shake with 50 milliliters of ether. Discard the aqueous layer, and wash the ether layer with approximately 30 milliliters of water. Discard the aqueous layer again and extract with approximately 50 milliliters of 0.1*N* sodium hydroxide. Obtain a spectrum of the 0.1*N* sodium hydroxide solution from 300 nanometers to 240 nanometers against a reagent blank. Treat about 15 milligrams of the cloxacillin working standard in the same manner. The sample is satisfactory if the spectrum obtained from the sample solution matches that of the standard solution with maximum at about 282 nanometers and minimum at about 257 nanometers.

(6) *Crystallinity.* Proceed as directed in § 436.203 of this chapter.

[40 FR 13888, Mar. 27, 1975, as amended at 50 FR 19922, May 13, 1985]

§ 540.114a Sterile benzathine cloxacillin.

(a) Requirements for certification—

(1) *Standards of identity, strength, quality, and purity.* Benzathine cloxacillin is the *N,N'*-dibenzyleth-ylenediamine salt of 5-methyl-3-(*o*-chlorophenyl)-4-isoxazolyl penicillin. It is so purified and dried that:

(i) Its potency is not less than 704 nor more than 821 micrograms of cloxacillin per milligram on an anhydrous basis.

(ii) It is sterile.

- (iii) [Reserved]
- (iv) Its moisture content is not more than 5.0 percent.
- (v) Its pH in an aqueous suspension containing 10 milligrams per milliliter is not less than 3.0 nor more than 6.5.
- (vi) It passes the identity test.
- (vii) It is crystalline.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, sterility, moisture, pH, identity, and crystallinity.

(ii) Samples required:

(a) For all tests except sterility: 10 packages, each containing approximately 300 milligrams.

(b) For sterility testing: 20 packages, each containing approximately 600 milligrams.

(b) *Tests and methods of assay—(1) Potency.* Use the microbiological agar diffusion assay method: Proceed in accordance with § 436.105 of this chapter, using the cloxacillin working standard as the standard of comparison and prepare the sample for assay as follows: Dissolve an accurately weighed portion of the sample in sufficient methanol to give a convenient stock solution. Immediately dilute an aliquot of this stock solution with solution 1 to the reference concentration of 5.0 micrograms of cloxacillin per milliliter estimated.

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(2) of that section, except use medium C in lieu of medium A, medium F in lieu of medium E, and during the period of incubation shake the tubes at least once daily.

(3) [Reserved]

(4) *Moisture.* Proceed in accordance with § 436.201 of this chapter.

(5) *pH.* Proceed in accordance with § 436.202 of this chapter, using an aqueous suspension prepared by adding 10 milligrams per milliliter.

(6) *Identity.* Transfer approximately 20 milligrams of the sample to a 50-milliliter Erlenmeyer flask. Add 5.0 milliliters of 5N sodium hydroxide and

heat in a steam bath 20 minutes. Cool. Transfer 1 milliliter to an extraction funnel; add approximately 10 milliliters of water and 1 milliliter of dilute sulfuric acid (1:2). Shake with 50 milliliters of ether. Discard the aqueous layer and wash the ether layer with approximately 30 milliliters of water. Discard the aqueous layer again and extract with approximately 50 milliliters of 0.1N sodium hydroxide. Obtain a spectrum of the 0.1N sodium hydroxide solution from 300 nanometers to 240 nanometers against a reagent blank. Treat about 15 milligrams of the cloxacillin working standard in the same manner. The sample is satisfactory if the spectrum obtained from the sample solution matches that of the standard solution with maximum at about 282 nanometers and minimum of about 257 nanometers.

(7) *Crystallinity.* Proceed as directed in § 436.203 of this chapter.

[40 FR 13888, Mar. 27, 1975, as amended at 50 FR 19922, May 13, 1985]

§ 540.119 Sodium dicloxacillin monohydrate capsules.

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality, and purity.* Sodium dicloxacillin monohydrate capsules are composed of sodium dicloxacillin monohydrate and one or more suitable diluents and lubricants. Each capsule contains sodium dicloxacillin monohydrate equivalent to 50, 100, 200, or 500 milligrams of dicloxacillin. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of dicloxacillin that it is represented to contain. The moisture content is not more than 5 percent. The sodium dicloxacillin monohydrate conforms to the requirements of § 440.19(a)(1) of this chapter.

(2) *Labeling.* It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The sodium dicloxacillin monohydrate used in making the batch for potency, moisture, pH, organic chlorine content, free chloride content, crystallinity, and identity.

(b) The batch for potency and moisture.

(ii) Samples required:

(a) The sodium dicloxacillin monohydrate used in making the batch: 10 containers, each containing not less than 500 milligrams.

(b) The batch: A minimum of 30 capsules.

(b) *Tests and methods of assay*—(1)

Potency—(i) *Sample preparation*. Place a representative number of capsules into a high-speed glass blender jar containing sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to give a stock solution of convenient concentration. Blend for 3 to 5 minutes. Remove an aliquot and further dilute with solution 1 to the reference concentration of 5 micrograms of dicloxacillin per milliliter (estimated) for the microbiological agar diffusion assay and to the prescribed concentration for the iodometric assay.

(ii) *Assay procedure*. Assay for potency by either of the following methods; however, the results obtained from the microbiological agar diffusion assay shall be conclusive.

(a) *Microbiological agar diffusion assay*. Proceed as directed in § 436.105 of this chapter.

(b) *Iodometric assay*. Proceed as directed in § 436.204 of this chapter.

(2) *Moisture*. Proceed as directed in § 436.201 of this chapter.

(c) *Conditions of marketing*—(1) *Specifications*. The drug is in capsule form and conforms to the certification requirements of paragraph (a) of this section.

(2) *Sponsor*. See No. 000856 in § 510.600(c) of this chapter.

(3) *Conditions of use*. (i) It is used in dogs in the treatment of pyoderma (pyogenic dermatitis) known to be due to penicillinase-producing staphylococci which have been shown to be sensitive to the drug.

(ii) It is administered to dogs at the rate of 5 milligrams to 10 milligrams per pound of body weight, three times daily. In severe cases the dose may be

increased to 25 milligrams per pound of body weight three times daily. Treatment should be continued for 24 to 48 hours after the animal has become afebrile or asymptomatic. The drug should be administered 1 to 2 hours before feeding to insure maximum absorption.

(iii) For use in the treatment of dogs only. Not for use in animals which are raised for food production.

(iv) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13888, Mar. 27, 1975, as amended at 50 FR 19922, May 13, 1985; 53 FR 27852, July 25, 1988]

§ 540.129 Potassium hetacillin oral dosage forms.

§ 540.129a Potassium hetacillin tablets.

(a) *Requirements for certification*—

(1) *Standards of identity, strength, quality, and purity*. Potassium hetacillin tablets are composed of potassium hetacillin with or without one or more suitable buffer substances, diluents, binders, lubricants, flavorings, and colorings. Each tablet contains an amount of potassium hetacillin equivalent to 50, 100, or 200 milligrams of ampicillin. Its potency is satisfactory if it contains not less than 90 percent and not more than 120 percent of the number of milligrams of ampicillin that it is represented to contain. The moisture content is not more than 5 percent. Tablets shall disintegrate within 30 minutes. The potassium hetacillin used conforms to the requirements of § 440.29 of this chapter.

(2) *Labeling*. It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter.

(3) *Requests for certification; samples*. In addition to complying with the requirements of section 512(b) of the Federal Food, Drug, and Cosmetic Act and § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The potassium hetacillin used in making the batch for potency, moisture, pH, potassium hetacillin content, identity, and crystallinity.

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(b) The batch for potency, moisture, and disintegration time.

(ii) Samples required:

(a) The potassium hetacillin used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch: A minimum of 36 tablets.

(b) *Tests and methods of assay*—(1) *Potency*. Proceed as directed for ampicillin in § 436.105 of this chapter, using the ampicillin working standard as the standard of comparison and preparing the sample for assay as follows: Place a representative number of tablets in a high-speed glass blender with sufficient 0.1M potassium phosphate buffer, pH 8.0 (solution 3), to give a stock solution of convenient concentration. Blend for 3 to 5 minutes. Further dilute an aliquot of the stock solution with solution 3 to the reference concentration of 0.1 microgram of ampicillin per milliliter (estimated).

(2) *Moisture*. Proceed as directed in § 436.201 of this chapter.

(3) *Disintegration time*. Proceed as directed in § 436.212 of this chapter, using the procedure described in § 436.212(e)(1) of this chapter.

(c) *Conditions of marketing*—(1) *Specifications*. The drug is in capsule or tablet form. The capsules conform to the certification requirements of § 540.129b, and the tablets conform to the certification requirements of paragraph (a) of this section.

(2) *Sponsor*. See No. 000856 in § 510.600(c) of this chapter.

(3) *Conditions of use*. (i) It is used in dogs and cats as a treatment against strains of organisms sensitive to potassium hetacillin and associated with respiratory tract infections, urinary tract infections, gastrointestinal infections, skin infections, soft tissue infections, and postsurgical infections.

(ii) Dosage is administered as follows:

(a) In dogs, administer twice daily at a minimum rate of 5 milligrams per pound of body weight. In severe infections the frequency of the dosage may be increased to three times daily, or alternatively, the dosage may be increased to 10 milligrams per pound of body weight twice daily. For stubborn urinary tract infections, the dosage

may be increased to 20 milligrams per pound of body weight twice daily. Treatment should be continued for 48 to 72 hours after the animal has become afebrile or asymptomatic. The oral drug should be administered 1 to 2 hours prior to feeding to ensure maximum absorption.

In stubborn infections, therapy may be required for several weeks.

(b) In cats the recommended dosage is 50 milligrams twice daily. Treatment should be continued for 48 to 72 hours after the animal has become afebrile or asymptomatic. The oral drug should be administered in a fasting state to ensure maximum absorption. In stubborn infections, therapy may be required for several weeks.

(iii) For use in dogs and cats only. Not to be used in animals which are raised for food production.

(iv) For use only by or the order of a licensed veterinarian.

[40 FR 13888, Mar. 27, 1975, as amended at 50 FR 19922, May 13, 1985; 53 FR 27852, July 25, 1988]

§ 540.129b Potassium hetacillin capsules.

(a) *Requirements for certification*—

(1) *Standards of identity, strength, quality, and purity*. Potassium hetacillin capsules are composed of potassium hetacillin with or without one or more suitable diluents, lubricants, and drying agents. Each capsule contains an amount of potassium hetacillin equivalent to 50, 100, or 200 milligrams of ampicillin. Its potency is satisfactory if it contains not less than 90 percent and not more than 120 percent of the number of milligrams of ampicillin that it is represented to contain. The moisture content is not more than 3 percent. The potassium hetacillin used conforms to the requirements of § 440.29.

(2) *Labeling*. It shall be labeled in accordance with the requirements of §§ 540.129a and 510.55 of this chapter.

(3) *Requests for certification; samples*. In addition to complying with the requirements of section 512(b) of the Federal Food, Drug, and Cosmetic Act and § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The potassium hetacillin used in making the batch for potency, moisture, pH, potassium hetacillin content, identity, and crystallinity.

(b) The batch for potency and moisture.

(i) Samples required:

(a) The potassium hetacillin used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch: A minimum of 30 capsules.

(b) *Tests and methods of assay*—(1) *Potency*. Proceed as directed for ampicillin in § 436.105 of this chapter, using the ampicillin working standard as the standard of comparison and preparing the sample for assay as follows: Place a representative number of capsules in a high-speed glass blender with sufficient 0.1M potassium phosphate buffer, pH 8.0 (solution 3), to give a stock solution of convenient concentration. Blend for 3 to 5 minutes. Further dilute an aliquot of the stock solution with solution 3 to the reference concentration of 0.1 microgram of ampicillin per milliliter (estimated).

(2) *Moisture*. Proceed as directed in § 436.201 of this chapter.

(c) *Conditions of marketing*. The conditions of marketing of potassium hetacillin capsules are described in § 540.129a(c).

(40 FR 13888, Mar. 27, 1975, as amended at 50 FR 19922, May 13, 1985)

§ 540.129c Potassium hetacillin oral suspension.

(a) *Requirements for certification*—

(1) *Standards of identity, strength, quality, and purity*. Potassium hetacillin oral suspension is potassium hetacillin with one or more suitable and harmless colorings, flavorings and gelling agents suspended in a suitable and harmless non-aqueous vehicle. It contains in each milliliter an amount of potassium hetacillin equivalent to 50 milligrams of ampicillin. Its potency is satisfactory if it contains not less than 90 percent and not more than 120 percent of the number of milligrams of ampicillin it is represented to contain. Its moisture content is not more than 1.0 percent. Its pH is not less than 7.0 and not more than 9.0. It gives a positive identity test for hetacillin. The

potassium hetacillin used conforms to the requirements of § 440.29 of this chapter.

(2) *Labeling*. It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter.

(3) *Requests for certification; samples*. In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The potassium hetacillin used in making the batch for potency, moisture, pH, potassium hetacillin content, identity and crystallinity.

(b) The batch for potency, moisture, pH and identity.

(ii) Samples required:

(a) The potassium hetacillin used in making the batch, 10 packages, each containing approximately 300 milligrams.

(b) The batch: A minimum of eight immediate containers.

(b) *Tests and methods of assay*—(1) *Potency*. Proceed as directed for ampicillin in § 436.105 of this chapter, using the ampicillin working standard as the standard for comparison and preparing the sample for assay as follows: Place an accurately measured aliquot (usually 1 milliliter) into a high-speed glass blender jar, with sufficient 0.1 M potassium phosphate buffer, pH 8.0 (solution 3) to give a stock solution of convenient concentration. Blend 3 to 5 minutes. Further dilute an aliquot of the stock solution with solution 3 to the reference concentration of 0.1 microgram of ampicillin per milliliter (estimated).

(2) *Moisture*. Proceed as directed in § 436.201 of this chapter.

(3) *pH*. Proceed as directed in § 436.202 of this chapter, preparing the sample as follows: Transfer about 5.0 milliliters of the well shaken sample to a centrifuge tube. Add 10 milliliters of benzene, shake vigorously for 3 minutes and centrifuge at medium speed for 5 minutes. Carefully decant the benzene without disturbing the precipitate. Add 5 milliliters of carbon dioxide-free distilled water.

(4) *Hetacillin identity*. Proceed as directed in § 436.305 of this chapter preparing the sample solution as follows: Place 1.0 milliliter of the well shaken

sample into a 50-milliliter volumetric flask. Bring to volume with a 4:1 solution of acetone and 0.1 N hydrochloric acid.

(c) *Conditions of marketing*—(1) *Specifications*. The drug is in liquid form and conforms to the certification requirements of paragraph (a) of this section.

(2) *Sponsor*. See No. 000856 in § 510.600(c) of this chapter.

(3) *Conditions of use*. (i) It is used in dogs and cats as a treatment against strains of organisms susceptible to potassium hetacillin and associated with respiratory tract infections, urinary tract infections, gastrointestinal infections, skin infections, soft-tissue infections, and post-surgical infections.

(ii) Dosage is administered as follows:

(a) In dogs, administer twice daily at a minimum rate of 5 milligrams per pound of body weight. In severe infections the frequency of the dosage may be increased to three times daily, or alternatively, the dosage may be increased to 10 milligrams per pound of body weight twice daily. For stubborn urinary tract infections, the dosage may be increased to 20 milligrams per pound of body weight twice daily. Treatment should be continued for 48 to 72 hours after the animal has become afebrile or asymptomatic. The drug should be administered 1 to 2 hours prior to feeding to insure maximum absorption. In stubborn infections, therapy may be required for several weeks.

(b) In cats the recommended dosage is 50 milligrams twice daily. Treatment should be continued for 48 to 72 hours after the animal has become afebrile or asymptomatic. The drug should be administered 1 to 2 hours prior to feeding to insure maximum absorption. In stubborn infections, therapy may be required for several weeks.

(iii) For use in dogs and cats only. Not to be used in animals raised for food production.

(iv) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13888, Mar. 27, 1975, as amended at 50 FR 19922, May 13, 1985; 53 FR 27852, July 25, 1988]

§ 540.160 Dibenzylamine penicillin and potassium penicillin powder, buffered.

(a) *Requirements for certification*. (1) The requirements for certification for dibenzylamine penicillin and potassium penicillin powder, buffered, are described under § 440.160 of this chapter.

(2) When it is packaged for dispensing and intended for veterinary use, its label and labeling shall comply with all the requirements prescribed by § 440.160(a)(3) of this chapter, except that in lieu of the statement "Caution: Federal law prohibits dispensing without prescription," each package shall include information containing directions and warnings adequate for the veterinary use of the drug by the laity and the statement "Warning—Not for use in animals which are raised for food production."

(b) *Tests and methods of assay*. The tests and methods of assay for dibenzylamine penicillin and potassium penicillin powder, buffered, are described under § 440.160 of this chapter.

§ 540.173 Potassium phenoxymethyl penicillin oral dosage forms.

§ 540.173a Phenoxymethyl penicillin for oral suspension; potassium phenoxymethyl penicillin for oral solution.

(a) *Requirements for certification*. (1) The requirements for certification for phenoxymethyl penicillin for oral suspension and potassium phenoxymethyl penicillin for oral solution are described under § 440.171b(a) of this chapter.

(2) When phenoxymethyl penicillin for oral suspension and potassium phenoxymethyl penicillin for oral solution are packaged for dispensing and intended solely for veterinary use, their label and labeling shall comply with all the requirements prescribed by paragraph (c) of this section and § 510.55 of this chapter.

(b) *Tests and methods of assay*. The tests and methods of assay for phenoxymethyl penicillin for oral suspension are described under § 440.171b(b) of this chapter.

(c) *Conditions of marketing*—(1) *Specifications*. The drug consists of soluble granules which conform to the

certification requirements of paragraph (a) of this section.

(2) *Sponsor.* To No. 050604 in § 510.600(c) of this chapter, approval for 125 milligrams per 5 milliliters.

(3) *Conditions of use.* (i) The drug is administered to dogs and cats orally for the treatment of respiratory, urogenital, skin and soft tissue infections and septicemia caused by pathogens susceptible to potassium phenoxymethyl penicillin.¹

(ii) It is administered at a dosage of 10 to 15 milligrams per pound of body weight every 6 to 8 hours.¹

(iii) It should be administered 1 to 2 hours prior to feeding for maximum absorption.¹

(iv) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

[40 FR 13888, Mar. 27, 1975, as amended at 48 FR 30363, July 1, 1983; 48 FR 33480, July 22, 1983]

§ 540.173b Potassium phenoxymethyl penicillin tablets.

(a) *Requirements for certification.* The requirements for certification are described under § 440.173c of this chapter, except the labeling shall comply with the requirements of paragraph (c) of this section and § 510.55 of this chapter.

(b) *Tests and methods of assay.* The tests and methods of assay are described under § 440.173c of this chapter.

(c) *Conditions of marketing—(1) Specifications.* Each tablet contains potassium phenoxymethyl penicillin and conforms to the certification requirements of paragraph (a) of this section.

(2) *Sponsor.* To No. 050604 in § 510.600(c) of this chapter, approval for tablets containing 125 or 250 milligrams of the drug.

(3) *Conditions of use.* (i) The drug is administered to dogs and cats for the treatment of respiratory, urogenital, skin and soft tissue infections and sep-

ticemia caused by pathogens susceptible to potassium phenoxymethyl penicillin.¹

(ii) It is administered orally at a dosage of 10 to 15 milligrams per pound of body weight every 6 to 8 hours.¹

(iii) It should be administered 1 to 2 hours prior to feeding for maximum absorption.¹

(iv) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

[40 FR 13888, Mar. 27, 1975, as amended at 47 FR 16320, Apr. 16, 1982; 48 FR 30363, July 1, 1983]

§ 540.174 Procaine penicillin oral dosage forms.

§ 540.174a Buffered penicillin powder, penicillin powder with buffered aqueous diluent.

(a) *Requirements for certification.*

(1) The requirements for certification for buffered penicillin powder and penicillin powder with buffered aqueous diluent are described under § 440.180f of this chapter.

(2) When buffered penicillin powder and penicillin powder with buffered aqueous diluent are packaged for dispensing and intended solely for veterinary use: (i) Their labels and labeling shall comply with all the requirements prescribed by § 440.180f(a)(3) of this chapter, except that in lieu of the statement "Caution: Federal law prohibits dispensing without prescription", each package shall include information containing directions and warnings adequate for the veterinary use of the drug by the laity.

(ii) If it contains added vitamins or minerals, the labels shall bear the name and quantity of each such substance and a statement that such substances are present only for furnishing additional vitamins and minerals while animals are eating less feed.

(iii) If it is intended for use in animals raised for food production, it

¹These conditions are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

¹These conditions are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

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shall be used in accordance with paragraph (c) of this section.

(b) *Tests and methods of assay.* The tests and methods of assay for buffered penicillin powder are described under § 440.180f of this chapter.

(c) *Conditions of marketing—(1) Specifications.* Complies with the requirements for procaine penicillin found in paragraph (a) of this section or § 540.173b.

(2) *Sponsor.* [Reserved]

(3) *Special considerations.* The quantities of antibiotic in paragraph (c)(5) of this section refer to the activity of the master standard.

(4) *Related tolerances.* See § 556.510 of this chapter.

(5) *Conditions of use.* It is used in the drinking water of chickens as follows:

(i) *Amount per gallon.* 100,000 units. (a) *Indications for use.* For treatment of chronic respiratory disease (air-sac infection) and blue comb (nonspecific infectious enteritis).

(b) *Limitations.* As procaine penicillin; not for use in laying chickens; prepare fresh solution daily; withdraw 1 day before slaughter; as sole source of penicillin.

(ii) *Amount per gallon.* 50,000 to 100,000 units.

(a) *Indications for use.* For prevention of chronic respiratory disease (air-sac infection) and blue comb (nonspecific infectious enteritis).

(b) *Limitations.* As procaine penicillin; not for use in laying chickens; prepare fresh solution daily; withdraw 1 day before slaughter; as sole source of penicillin.

§ 540.181 Crystalline penicillin oral dosage forms.

§ 540.181a [Reserved]

§ 540.181b Potassium penicillin G in drinking water.

(a)—(b) [Reserved]

(c) *Conditions of marketing—(1) Specifications.* The drug contains 0.384 billion units of potassium penicillin G per container. Potassium penicillin G must conform to the specifications in § 540.280(a), except for sterility and pyrogens.

(2) *Sponsor.* See No. 017210 in § 510.600(c) of this chapter.

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(3) *Conditions of use.* (i) The drug is intended for use in turkeys for treatment of erysipelas caused by *Erysipelothrix insidiosus*.

(ii) It is administered in the drinking water of turkeys at the rate of 1,500,000 units per gallon of water for 5 days.

(iii) Concentrated stock solution prepared for use with medication proportioners must be prepared fresh every 24 hours. Recommended use levels (gravity flow watering system) must be prepared fresh every 12 hours. For best results treatment should be started at the first sign of infection.

(iv) Discontinue treatment at least 1 day prior to slaughter of the turkeys. Not to be used in turkeys producing eggs for human consumption.

[40 FR 13888, Mar. 27, 1975, as amended at 50 FR 41490, Oct. 11, 1985; 53 FR 40729, Oct. 18, 1988]

Subpart B—Implantation or Injectable Dosage Forms

§ 540.203 Sterile amoxicillin trihydrate for suspension.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Sterile amoxicillin trihydrate for suspension is a dry mixture of amoxicillin trihydrate and one or more suitable and harmless buffer substances, stabilizers, suspending agents, and preservatives. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the labeled amount of amoxicillin. It is sterile. It is nonpyrogenic. Its moisture content is not less than 11.0 percent and not more than 14.0 percent. When reconstituted as directed in the labeling, its pH is not less than 5.0 and not more than 7.0. The amoxicillin trihydrate used conforms to the requirements of § 539.3 of this chapter.

(2) *Labeling.* It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter, and in addition, this drug shall be labeled "sterile amoxicillin for suspension, veterinary".

(3) *Requests for certification; samples.* In addition to complying with the

requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The amoxicillin trihydrate used in making the batch for potency, moisture, pH, amoxicillin content, concordance, crystallinity, and identity.

(b) The batch for potency, sterility, pyrogens, moisture, and pH.

(ii) Samples required:

(a) The amoxicillin trihydrate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch:

(1) For all tests except sterility: A minimum of 12 immediate containers.

(2) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) Tests and methods of assay—(1)

Potency—(i) *Sample preparation*. Reconstitute as directed in the labeling. Using a suitable hypodermic needle and syringe, remove all of the withdrawable contents if the container is represented as a single-dose container or, if the labeling specifies the amount of potency in a given volume of the resultant preparation, remove an accurately measured representative portion from each container. Dilute the resultant solution with 0.1 M potassium phosphate buffer, pH 8.0 (solution 3), for the microbiological agar diffusion, assay, or distilled water for the iodometric assay, to give a stock solution of convenient concentration.

(ii) *Assay procedure*. Use either of the following methods; however, the results obtained from the iodometric assay shall be conclusive.

(a) *Microbiological agar diffusion assay*. Proceed as directed in § 436.105 of this chapter, diluting an aliquot of the stock solution with solution 3 to the reference concentration of 0.1 microgram of amoxicillin per milliliter (estimated).

(b) *Iodometric assay*. Proceed as directed in § 436.204 of this chapter, except in paragraph (d) of that section, add 3 drops of 1.2N hydrochloric acid to both the sample and working standard solutions after the addition of 0.01N iodine solution. Dilute an aliquot of the stock solution with dis-

tilled water to the prescribed concentration.

(2) *Sterility*. Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(2) of that section, except use medium C in lieu of medium A, medium F in lieu of medium E, and during the period of incubation shake the tubes at least once daily.

(3) *Pyrogens*. Proceed as directed in § 436.32(f) of this chapter, using a solution containing 20 milligrams of amoxicillin per milliliter.

(4) [Reserved]

(5) *Moisture*. Proceed as directed in § 436.201 of this chapter.

(6) *pH*. Proceed as directed in § 436.202 of this chapter, using the solution obtained when the product is reconstituted as directed in the labeling.

(c) *Conditions of marketing*—(1)(i) *Specifications*. Each vial contains 3 grams of amoxicillin activity as the trihydrate. It is reconstituted with sterile water for injection USP to the concentration of 100 or 250 milligrams per milliliter.

(ii) *Sponsor*. See 000029 in § 510.600(c) of this chapter.

(iii) *Conditions of use in dogs and cats*—(a) *Amount*. 5 milligrams per pound of body weight daily.

(b) *Indications for use*—(1) *Dogs*: Use for the treatment of infections caused by susceptible strains of organisms as follows: Respiratory infections (tonsillitis, tracheobronchitis) due to *Staphylococcus aureus*, *Streptococcus* spp., *E. coli*, and *Proteus mirabilis*; genitourinary infections (cystitis) due to *Staphylococcus aureus*, *Streptococcus* spp., *E. coli*, and *Proteus mirabilis*; gastrointestinal infections (bacterial gastroenteritis) due to *Staphylococcus aureus*, *Streptococcus* spp., *E. coli*, and *Proteus mirabilis*; soft tissue infections (abscesses, lacerations, and wounds) due to *Staphylococcus aureus*, *Streptococcus* spp., *E. coli*, and *Proteus mirabilis*.

(2) *Cats*: Use for the treatment of infections caused by susceptible strains of organisms as follows: Upper respiratory infections due to *Staphylococcus*

aureus, *Staphylococcus* spp., *Streptococcus* spp., *Hemophilus* spp., *E. coli*, *Pasteurella* spp., and *Proteus mirabilis*; genitourinary infections (cystitis) due to *Staphylococcus aureus*, *Streptococcus* spp., *E. coli*, *Proteus mirabilis*, and *Corynebacterium* spp.; gastrointestinal infections due to *E. coli*, *Proteus* spp., *Staphylococcus* spp., and *Streptococcus* spp.; skin and soft tissue infections (abscesses, lacerations, and wounds) due to *Staphylococcus aureus*, *Staphylococcus* spp., *Streptococcus* spp., *E. coli*, and *Pasteurella multocida*.

(c) *Limitations*. Administer once daily for up to 5 days by intramuscular or subcutaneous injection. Treatment should be continued for 48 hours after the animal has become afebrile or asymptomatic. If no improvement is seen within 5 days, review the diagnosis and change therapy. As with all antibiotics, appropriate in vitro culturing and susceptibility testing of samples taken before treatment should be conducted. For use in dogs and cats only. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(2)(i) *Specifications*. Each vial contains 25 grams of amoxicillin activity as the trihydrate. The vial is reconstituted with sterile water for injection, USP to a concentration of 250 milligrams per milliliter.

(ii) *Sponsor*. See 000029 in § 510.600(c) of this chapter.

(iii) *Related tolerances*. See § 556.38 of this chapter.

(iv) *Conditions of use in cattle*—(a) *Amount*. 3 to 5 milligrams per pound of body weight once a day according to the animal being treated, the severity of infection, and the animal's response.

(b) *Indications for use*. Treatment of diseases due to amoxicillin-susceptible organisms as follows: Respiratory tract infections (shipping fever, pneumonia) due to *Pasteurella multocida*, *P. hemolytica*, *Hemophilus* spp., *Staphylococci* spp., and *Streptococci* spp. and acute necrotic pododermatitis (foot rot) due to *Fusobacterium necrophorum*.

(c) *Limitations*. Administer once daily for up to 5 days by intramuscular or subcutaneous injection. Treat-

ment should be continued for 48 to 72 hours after the animal has become afebrile or asymptomatic. Do not continue treatment beyond 5 days. Treated animals must not be slaughtered for food during treatment and for 7 days after the last treatment. As with all antibiotics, appropriate in vitro culturing and susceptibility testing of samples taken before treatment should be conducted. Milk from treated cows must not be used for human consumption during treatment or for 96 hours (8 milkings) after last treatment. Maximum volume per injection site should not exceed 30 milliliters. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(Secs. 507, 512(n), 701(f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 360b(n), 371(f) and (g)))

(43 FR 38001, Aug. 25, 1978, as amended 47 FR 39813, Sept. 10, 1982; 47 FR 445 Oct. 8, 1982; 49 FR 3460, Jan. 27, 1984; 53 FR 19922, May 13, 1988; 53 FR 40059 Oct. 13, 1988)

§ 540.207 Sterile ampicillin trihydrate injection and injectable dosage form

§ 540.207a Sterile ampicillin trihydrate suspension.

(a) *Requirements for certification*
(1) *Standards of identity, strength, quality, and purity*. Sterile ampicillin trihydrate suspension is ampicillin trihydrate in a suitable and harmless base. It may contain one or more suitable and harmless preservatives, antioxidants, and complexing or suspending agents. It contains, in each milliliter, an amount of ampicillin trihydrate equivalent to 150 or 200 milligrams of ampicillin. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of ampicillin that it is represented to contain. It is sterile. Its moisture content is not more than 4.0 percent. The ampicillin trihydrate used conforms to the requirements of § 440.7a(a)(1) of this chapter.

(2) *Labeling*. It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) The results of tests and assays on:

(a) The ampicillin trihydrate used in making the batch for potency, pyrogens, loss on drying, pH, ampicillin content, concordance, crystallinity, and identity.

(b) The batch for potency, sterility, and moisture.

(ii) Samples required:

(a) The ampicillin trihydrate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch:

(1) For all tests except sterility: A minimum of 5 immediate containers.

(2) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay—(1) Potency.* Use either of the following methods; however, the results obtained from the microbiological agar diffusion assay shall be conclusive:

(i) *Microbiological agar diffusion assay.* Proceed in accordance with § 436.105 of this chapter, preparing the sample as follows: Using a 22-gage hypodermic needle and suitable syringe, place an accurately measured representative portion of the sample (usually 1 milliliter) into a high-speed glass blender jar. Add 1.0 milliliter of polysorbate 80 and sufficient 0.1M potassium phosphate buffer, pH 8.0 (solution 3) to give a stock solution of convenient concentration. Blend for 3 to 5 minutes. Further dilute with solution 3 to the reference concentration of 0.1 microgram of ampicillin per milliliter.

(ii) *Iodometric assay.* Proceed as directed in § 436.204 of this chapter, except in paragraph (d) of that section, add 3 drops of 1.2N hydrochloric acid to both the sample and working standard solutions after the addition of 0.01N iodine solution. Prepare the sample as follows: Using a suitable syringe and needle, transfer a 2.5-milliliter portion of the sample to a separatory funnel containing 100 milliliters of diethyl ether. Extract twice with 100 milliliters of 0.2N hydrochloric

acid. Collect the extracts in a 500-milliliter volumetric flask. Bring to volume with distilled water to obtain a concentration of 1 milligram per milliliter (estimated).

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(2) of that section, except use medium C in lieu of medium A and medium F in lieu of medium E. During the period of incubation, shake the tubes at least once daily.

(3) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(c) *Conditions of marketing—(1) Specifications.* Sterile ampicillin suspension contains 200 milligrams of ampicillin (as ampicillin trihydrate) per milliliter of nonaqueous vehicle and conforms to the requirements of paragraph (a) of this section.

(i) *Sponsor.* See No. 053501 in § 510.600(c) of this chapter.

(ii) *Related tolerances.* See § 556.40 of this chapter.

(iii) *Conditions of use—(a) In calves.* (1) Administer intramuscularly for the treatment of bacterial enteritis caused by *E. coli* and bacterial pneumonia caused by *Pasteurella spp.* susceptible to ampicillin.

(2) For treatment of enteritis: 3 milligrams per pound of body weight, once or twice daily, for up to 3 days; treatment of pneumonia: 3 milligrams per pound of body weight, twice daily, for up to 3 days.

(3) It is not for use in other animals raised for food production.

(4) Treated animals must not be slaughtered for food use during treatment or for 9 days after the last treatment.

(5) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(b) *In dogs.* (1) Administer intramuscularly for the treatment of respiratory tract infections due to *E. coli*, *Pseudomonas spp.*, *Proteus spp.*, *Staphylococcus spp.*, and *Streptococcus spp.*; tonsillitis due to *E. coli*, *Pseudomonas spp.*, *Streptococcus spp.*, and *Staphylococcus spp.*; generalized infections (septicemia) associated with abscesses, lacerations, and wounds due to *Staphylococcus spp.* and *Streptococcus spp.*

(2) Administer at a dose of 3 to 6 milligrams per pound of body weight once or twice daily until at least 48 hours after the animal's temperature has returned to normal and other signs of infection have subsided. Usual treatment is 3 to 5 days.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(c) *In cats.* (1) Administer intramuscularly or subcutaneously for the treatment of generalized infections (septicemia) associated with abscesses, lacerations, and wounds due to *Staphylococcus spp.*, *Streptococcus spp.*, and *Pasteurella spp.*

(2) Administer at a dose of 5 to 10 milligrams per pound of body weight once or twice daily until at least 48 hours after the animal's temperature has returned to normal and other signs of infection have subsided. Usual treatment is 3 to 5 days.

(3) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(d) *In swine.* (1) Administer intramuscularly for the treatment of bacterial enteritis (colibacillosis) caused by *E. coli* and bacterial pneumonia caused by *Pasteurella spp.* susceptible to ampicillin.

(2) Administer at a dose of 3 milligrams per pound of body weight, once or twice daily, for up to 3 days.

(3) Treated animals must not be slaughtered for food use during treatment or for 15 days after the last treatment.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(2) *Specifications.* The drug contains 150 milligrams of ampicillin (as ampicillin trihydrate) per milliliter of nonaqueous vehicle and conforms to the requirements of paragraph (a) of this section.

(i) *Sponsor.* See No. 000029 in § 510.600(c) of this chapter.

(ii) *Related tolerances.* See § 556.40 of this chapter.

(iii) *Conditions of use—(a) In dogs.* Administer at a dose of 3 to 5 milligrams of ampicillin per pound of body weight, once a day for up to 4 days.

(1) *Indications for use.* It is used in the treatment of bacterial infections

of the upper respiratory tract (tonsillitis) due to *Streptococcus spp.*, *Staphylococcus spp.*, *E. coli*, *Proteus spp.*, and *Pasteurella spp.*, and soft tissue infections (abscesses, lacerations, and wounds) due to *Staphylococcus spp.*, *Streptococcus spp.*, and *Escherichia coli*, when caused by susceptible organisms.

(2) *Limitations.* Administer intramuscularly. If continued treatment is indicated, oral dosage is recommended. As with all antibiotics, appropriate in vitro culturing and susceptibility tests of samples taken before treatment are recommended. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(Secs. 507, 512(n), 701(f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371(f) and (g)))

[40 FR 13888, Mar. 27, 1975, as amended at 41 FR 10063, Mar. 9, 1976; 43 FR 4602, Feb. 3, 1978; 45 FR 81739, Dec. 12, 1980; 48 FR 3461, Jan. 27, 1984; 50 FR 19922, May 13, 1985; 50 FR 41490, Oct. 11, 1985]

§ 540.207b Sterile ampicillin trihydrate for suspension.

(a) *Requirements for certification—*
(1) *Standards of identity, strength, quality, and purity.* Sterile ampicillin trihydrate for suspension is a dry mixture of ampicillin trihydrate and one or more suitable and harmless buffer substances, stabilizers, suspending agents, and preservatives. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of ampicillin that it is represented to contain. It is sterile. It is nonpyrogenic. Its loss on drying is not less than 11.4 percent and not more than 14.0 percent. When reconstituted as directed in the labeling, its pH is not less than 5.0 and not more than 7.0. The ampicillin trihydrate used conforms to the requirements of § 440.7a of this chapter.

(2) *Labeling.* It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter, and in addition, this drug shall be labeled "sterile ampicillin for suspension, veterinary".

(3) *Requests for certification; samples.* In addition to complying with the

requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The ampicillin trihydrate used in making the batch for potency, loss on drying, pH, ampicillin content, concordance, crystallinity, and identity.

(b) The batch for potency, sterility, pyrogens, loss on drying, and pH.

(ii) Samples required:

(a) The ampicillin trihydrate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch:

(1) For all tests except sterility: A minimum of 12 immediate containers.

(2) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) Tests and methods of assay—(1)

Potency—(i) *Sample preparation*. Reconstitute as directed in the labeling. Using a suitable hypodermic needle and syringe, remove all of the withdrawable contents if it is represented as a single dose container or, if the labeling specifies the amount of potency in a given volume of the resultant preparation, remove an accurately measured representative portion from each container. Dilute the resultant solution with 0.1M potassium phosphate buffer, pH 8.0 (solution 3), for the microbiological agar diffusion assay, or distilled water for the iodometric assay, to give a stock solution of convenient concentration.

(ii) *Assay procedure*. Use either of the following methods; however, the results obtained from the microbiological agar diffusion assay shall be conclusive.

(a) *Microbiological agar diffusion assay*. Proceed as directed in § 436.105 of this chapter, diluting an aliquot of the stock solution with solution 3 to the reference concentration of 0.1 microgram of ampicillin per milliliter (estimated).

(b) *Iodometric assay*. Proceed as directed in § 436.204 of this chapter, except in paragraph (d) of that section, add 3 drops of 1.2N hydrochloric acid to both the sample and working standard solutions after the addition of 0.01N iodine solution. Dilute an aliquot of the stock solution with dis-

tilled water to the prescribed concentration.

(2) *Sterility*. Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section, except in lieu of paragraph (e)(1)(i)(a), prepare the sample for test as follows: From each of 10 immediate containers, aseptically transfer approximately 300 milligrams of sample into a sterile 500-milliliter Erlenmeyer flask containing approximately 400 milliliters of diluting fluid D. Add at least 200,000 Levy units¹ of penicillinase. Repeat the process using 10 additional containers. Swirl both of the stoppered flasks to completely solubilize the suspension prior to filtration and proceed as directed in paragraph (e)(1)(ii) of that section. If the formulation cannot be filtered, proceed as directed in § 436.20(e)(2), except use medium B in lieu of medium A and add at least 40,000 Levy units of penicillinase to both medium B and medium E.

(3) *Pyrogens*. Proceed as directed in § 436.32(f) of this chapter, using a solution containing 20 milligrams of ampicillin per milliliter.

(4) [Reserved]

(5) *Loss on drying*. Proceed as directed in § 436.200(a) of this chapter.

(6) *pH*. Proceed as directed in § 436.202 of this chapter, using the solution obtained when the product is reconstituted as directed in the labeling.

(c) *Conditions of marketing*—(1) *Specifications*. Sterile ampicillin trihydrate for suspension conforms to the standards of identity, strength, quality, and purity prescribed by paragraph (a) of this section.

(2) *Sponsor*. See No. 000856 in § 510.600(c) of this chapter.

(3) *Conditions of use*. (i) It is used in dogs and cats as a treatment against strains of organisms susceptible to ampicillin and associated with respiratory tract infections, urinary tract infections, gastrointestinal infections, skin

¹ One Levy unit of penicillinase inactivates 59.3 units of penicillin G in 1 hour at 25° C. and at a pH of 7.0 in a phosphate buffered solution of a pure alkali salt of penicillin G when the substrate is in sufficient concentration to maintain a zero order reaction.

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infections, soft tissue infections, and postsurgical infections.

(ii) Dosage is administered to dogs and cats at 3 milligrams per pound of body weight twice daily by subcutaneous or intramuscular injection. Treatment should be continued for 48 to 72 hours after the animal has become afebrile or asymptomatic.

(iii) It is used in cattle in the treatment of respiratory tract infection caused by organisms susceptible to ampicillin trihydrate, bacterial pneumonia (shipping fever, calf pneumonia, and bovine pneumonia) caused by *Aerobacter* spp., *Klebsiella* spp., *Staphylococcus* spp., *Streptococcus* spp., *Pasteurella multocida*, and *E. coli*.

(iv) It is administered to cattle at a dosage level of 2 to 5 mg/lb of body weight once daily by intramuscular injection.

(v) Do not treat cattle for more than 7 days. Milk from treated cows must not be used for food during treatment, and for 48 hours (4 milkings) after the last treatment. Treated cattle must not be slaughtered for food during treatment, and for 144 hours (6 days) after the last treatment.

(vi) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(Secs. 507, 512(n), 701(f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371(f) and (g)))

[40 FR 13888, Mar. 27, 1975, as amended at 49 FR 3461, Jan. 27, 1984; 50 FR 19922, May 13, 1985; 53 FR 27852, July 25, 1988]

§ 540.209 Ampicillin sodium for aqueous injection.

(a) *Requirements for certification.* The drug is sterile ampicillin packaged for dispensing. The requirements for certification are described in § 440.9a(a) of this chapter, except that the drug is labeled in accordance with requirements of paragraph (c) of this section and § 510.55 of this chapter.

(b) *Tests and methods of assay.* The tests and methods of assay for sterile ampicillin sodium are described in § 440.9a(b) of this chapter.

(c) *Conditions of marketing—(1) Specifications.* Complies with the requirements of paragraph (a) of this section. Each vial contains 3 grams of

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ampicillin which, when reconstituted according to directions, will provide a solution containing 300 milligrams of ampicillin per milliliter.

(2) *Sponsor.* See No. 000029 in § 510.600(c) of this chapter.

(3) *Conditions of use in horses—(1) Amount:* 3 milligrams per pound of body weight twice daily.

(ii) *Indications for use.* Treatment of respiratory tract infections (pneumonia and strangles) due to *Staphylococcus* spp., *E. coli*, and *Proteus mirabilis*, and skin and soft tissue infections (abscesses and wounds) due to *Staphylococcus* spp., *Streptococcus* spp., *E. coli*, and *Proteus mirabilis*, when caused by susceptible organisms.

(iii) *Limitations.* The drug may be administered either intravenously or intramuscularly. Treatment should be continued 48 hours after all symptoms have subsided. If no response is seen in 4 to 5 days, reevaluate diagnosis. Not for use in horses or other animals which are raised for food production. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[42 FR 8, Jan. 3, 1978]

§ 540.255 Benzathine penicillin G implantation and injectable dosage forms.

§ 540.255a Sterile benzathine penicillin G suspension.

(a) *Requirements for certification.* The requirements for certification for benzathine penicillin G for aqueous injection for veterinary use are described under § 440.255b of this chapter, with the following exceptions:

(1) *Packaging.* It need not be packaged for dispensing in immediate containers of colorless transparent glass. If it is the aqueous suspension of the drug, conspicuously labeled for veterinary use, the container is exempt from the 10-milliliter-maximum requirement prescribed by § 440.255b(a)(2) of this chapter.

(2) *Labeling.* When it is packaged for dispensing and intended solely for veterinary use, its label and labeling shall comply with all requirements prescribed by § 440.255b(a)(3) of this chapter, except that in lieu of the requirements of § 201.100 of this chapter

ter, it shall be labeled in accordance with the requirements prescribed by § 201.105 of this chapter, issued under section 502(f) of the act.

(b) *Tests and methods of assay.* The tests and methods of assay for benzathine penicillin G for aqueous injection are described under § 440.255b of this chapter.

(c) *Conditions of marketing—(1) Specifications.* Meets the specifications in paragraph (a) of this section.

(2) *Sponsor.* See No. 000008 in § 310.600(c) of this chapter.

(3) *Conditions of use.* (i) It is used for the treatment of bacterial infections susceptible to penicillin G in horses and dogs.¹

(ii) Inject intramuscularly in horses at 4,000 units per pound of body weight. Inject intramuscularly or subcutaneously in dogs at 12,000 to 24,000 units per pound of body weight. The dosage should be repeated in 48 hours.¹

(iii) Not to be used in animals intended for food purposes.¹

(iv) Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

§ 540.255b [Reserved]

§ 540.255c Sterile benzathine penicillin G and procaine penicillin G suspension.

(a) *Requirements for certification.* The requirements for certification for benzathine penicillin G and procaine penicillin for aqueous injection are described under § 440.255c of this chapter.

(b) *Tests and methods of assay.* The tests and methods of assay for benzathine penicillin G and procaine penicillin for aqueous injection are described in § 440.255c of this chapter, except that if the drug contains procaine hydrochloride, total potency, benzathine penicillin G content, and procaine penicillin G content are determined as follows:

(1) *Total potency.* Place one dose of the suspension in each of two centrifuge tubes. Label one tube "sample" and the other "blank." Add 9.0 milliliters of 20-percent sodium sulfate solution to each tube and mix well. Centrifuge them at 10,000 r/min for 15 minutes or until a clear supernatant solution is obtained. Pour the supernatant solution from the sample tube into a 50-milliliter volumetric flask and dilute to mark with 1 percent pH 6.0 buffer. Determine the amount of penicillin in this flask by the iodometric assay procedure as directed in § 436.204 of this chapter. Wash the penicillin residue from the tube labeled "sample" into a 200-milliliter volumetric flask quantitatively with about 150 milliliters of water. Add 10 milliliters of 1.0N sodium hydroxide and allow to stand for 15 minutes. Acidify the solution with 10 milliliters of 1.2N hydrochloric acid and dilute to mark with water. Determine the amount of penicillin in this solution by the iodometric assay procedure. Use as a blank a suspension prepared by discarding the supernatant from the tube labeled "blank," washing the penicillin residue into a 200-milliliter volumetric flask, and making to mark with water. The total potency of the dose is the sum of the penicillin in the sample supernatant solution and in the insoluble residue of the sample.

(2) *Procaine penicillin content.* Transfer 5.0 milliliters of the solution from the 200-milliliter volumetric flask containing the residue from the "sample" tube to a 50-milliliter volumetric flask and make to mark with water. Assay 2.0 milliliters of the solution by the Bratton-Marshall method. The amount of procaine penicillin is the sum of the amount of penicillin in the sodium sulfate supernatant solution and the amount of penicillin determined by the Bratton-Marshall method.

(3) *Benzathine penicillin content.* The amount of benzathine penicillin is the difference between the total potency and the amount of procaine penicillin.

(c) *Conditions of marketing—(1) Specifications.* Meets the specifications in paragraph (a) of this section. Each milliliter contains 150,000 units

¹ These conditions are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 314.111 of this chapter, but may require bioequivalency and safety information.

of benzathine penicillin G and 150,000 units of procaine penicillin G in aqueous suspension.¹

(2) *Sponsors.* (i) See Nos. 000008, 000856, 000029, 000856, 010271, and 010515 in § 510.600(c) of this chapter for the conditions of use in paragraph (c)(4)(i) of this section.

(ii) See Nos. 000029, 000856 and 010271 in § 510.600(c) of this chapter for the conditions of use in paragraph (c)(4)(ii) of this section.

(iii) See Nos. 000069 and 010515 in § 510.600(c) of this chapter for the conditions of use in paragraph (c)(4)(iii) of this section.

(3) *Related tolerances.* See § 556.510 of this chapter.

(4) *Conditions of use.* (i) It is used in horses, dogs, and beef cattle for the treatment of bacterial infections susceptible to penicillin G. The dosage given should be repeated in 48 hours. Restricted to use by or on the order of a licensed veterinarian.¹

(a) Inject intramuscularly in horses at 2 milliliters per 150 pounds of body weight. Do not use in horses intended for food purposes.¹

(b) Inject intramuscularly or subcutaneously in dogs at 1 milliliter per 10 to 25 pounds of body weight.¹

(c) Inject beef cattle subcutaneously only at 2 milliliters per 150 pounds of body weight. Treatment should be limited to two doses. Not to be used in beef cattle within 30 days of slaughter.¹

(ii) It is used in beef cattle for the treatment of bacterial pneumonia (*Streptococcus* spp., *Corynebacterium pyogenes*, *Staphylococcus aureus*); upper respiratory infections such as rhinitis or pharyngitis (*Corynebacterium pyogenes*); blackleg (*Clostridium chauvoei*); and for prophylaxis of bovine shipping fever in 300 to 500 pound beef calves.¹

(a) Inject subcutaneously 2 milliliters per 150 pounds of body weight. Repeat dosage in 48 hours. Limit treatment to two doses.¹

(b) Not for use within 30 days of slaughter.¹

¹ These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter.

(iii) It is used in beef cattle for treatment of bacterial pneumonia (shipping fever) (*Streptococcus* spp., *Corynebacterium pyogenes*, *Staphylococcus aureus*); upper respiratory infections such as rhinitis or pharyngitis (*Corynebacterium pyogenes*); and blackleg (*Clostridium chauvoei*).

(a) Inject subcutaneous 2 milliliters per 150 pounds of body weight. Repeat dosage in 48 hours. Limit treatment to two doses.

(b) Not for use within 30 days of slaughter.

[40 FR 13888, Mar. 27, 1975, as amended 40 FR 30639, July 22, 1975; 43 FR 117 Mar. 21, 1978; 47 FR 31865, July 23, 1982; FR 24872, 24873, June 3, 1983; 49 FR 196 May 9, 1984; 49 FR 44750, Nov. 9, 1984; FR 27852, July 25, 1988]

§ 540.261 Diethylaminoethyl ester penicillin G hydriodide for aqueous injection (penicillin G diethylaminoethyl ester hydriodide for aqueous injection).

(a) *Requirements for certification.* (1) The requirements for certification for diethylaminoethyl ester penicillin G hydriodide for aqueous injection (penicillin G diethylaminoethyl ester hydriodide for aqueous injection) are described under § 440.261 of this chapter.

(2) When it is packaged for dispensing and intended solely for veterinary use, its label and labeling shall comply with all the requirements prescribed by § 440.261(a)(3) of this chapter except that in lieu of the statement "Caution: Federal law prohibits dispensing without prescription", each package shall include information containing directions and warnings adequate for the veterinary use of the drug by the laity and the statement "Warning—Not for use in animals which are raised for food production".

(b) *Tests and methods of assay.* Tests and methods of assay for diethylaminoethyl ester penicillin G hydriodide for aqueous injection (penicillin G diethylaminoethyl ester hydriodide for aqueous injection) are described under § 440.261 of this chapter.

§ 540.274 Procaine penicillin G implantation and injectable dosage forms.

§ 540.274a Procaine penicillin for aqueous injection.

(a) Requirements for certification.

(1) The requirements for certification for procaine penicillin for aqueous injection are described under § 440.274b of this chapter.

(2) When procaine penicillin for aqueous injection is packaged for dispensing and intended solely for veterinary use, its label and labeling shall comply with all the following requirements:

(i) If it does not contain cortisone or a derivative of cortisone, its label and labeling shall comply with all of the requirements prescribed by § 440.274b(a)(3) of this chapter, except in lieu of the statement "Caution: Federal law prohibits dispensing without prescription", each package shall include information containing directions and warnings adequate for the veterinary use of the drug by the laity in all cases except those in which the veterinary prescription statement is required by regulations under this Subchapter E. In those cases, the veterinary prescription statement shall comply with the requirements prescribed by § 201.105 of this chapter.

(ii) If it contains cortisone or a derivative of cortisone, the label and labeling of each package shall conform with the requirements prescribed by § 201.105 of this chapter and with the requirements of § 510.55 of this chapter.

(iii) If it is intended for use in animals raised for food production, it shall be used in accordance with paragraph (c) of this section.

(b) Tests and methods of assay. The tests and methods of assay for procaine penicillin for aqueous injection are described under § 440.274b of this chapter.

(c) Conditions of marketing—(1) Specifications. Complies with the requirements of paragraph (a) of this section.

(2) Sponsor. [Reserved]

(3) Special considerations. (i) The labeling shall bear the statement "Warning—The use of this drug must be discontinued for 5 days before

treated animals are slaughtered for food."

(ii) If the drug is intended for use in animals producing milk for human consumption, the labeling shall also bear the statement "Milk that has been taken from animals during treatment and for — hours (— milkings) after the latest treatment must not be used for food", the blanks being filled with the figures 96 and 8 respectively, unless the sponsor of the drug has submitted the results of tests and assays demonstrating that residues of the drug in milk from treated animals persist for a shorter period of time and the shorter period is authorized by the Commissioner.

(iii) If the drug is intended for use in poultry, the labeling shall bear a statement that the drug is not to be used in birds producing eggs for human consumption.

(4) Related tolerances. See § 556.510 of this chapter.

(5) Conditions of use. As an intramuscular injection in food-producing animals in an amount not to exceed 2,000 units per pound of body weight per day.

§ 540.274b Procaine penicillin G aqueous suspension.

(a) Requirements for certification. The requirements for certification for procaine penicillin G aqueous suspension are described under § 540.274a.

(b) Tests and methods of assay. The tests and methods of assay for procaine penicillin G aqueous suspension are described under § 540.274a.

(c) Conditions of marketing—(1) [Reserved]

(2)(i) Specifications. The drug conforms to the requirements prescribed by § 540.274a. Each milliliter contains 300,000 units of penicillin activity.

(ii) Sponsor. See No. 053501 in § 510.600(c) of this chapter.

(iii) Conditions of use—(a) Dogs and cats—(1) Amount. 10,000 units per pound of body weight daily at 24-hour intervals.¹

¹ These conditions are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness

Continued

(2) *Indications for use.* For intramuscular injection in dogs and cats in treatment of infections caused by penicillin-sensitive organisms.¹

(3) *Limitations.* For intramuscular use only. Continue treatment at least 48 hours after symptoms disappear. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(b) *Cattle, sheep, swine, and horses—*
(1) *Amount.* 3,000 units per pound of body weight (1 milliliter per 100 pounds body weight) daily.¹

(2) *Indications for use.* For treatment of cattle and sheep for bacterial pneumonia (shipping fever) caused by *Pasteurella multocida*; swine for erysipelas caused by *Erysipelothrix insidiosa*; and horses for strangles caused by *Streptococcus equi*.¹

(3) *Limitations.* Administer by deep intramuscular injection. Continue treatment at least 48 hours after symptoms disappear but do not exceed 7 days of treatment in nonlactating dairy and beef cattle, sheep, and swine, or 5 days in lactating cattle. Milk that has been taken during treatment and for 48 hours (four milkings) after the last treatment must not be used for food. Discontinue treatment for the following number of days before slaughter: nonruminating cattle (calves)—7; all other cattle—4; sheep—8; and swine—6. Not for use in horses intended for food.

(3)(i) *Specifications.* The drug conforms to the requirements prescribed by § 540.274a. Each milliliter contains 300,000 units of penicillin activity.

(ii) *Sponsor.* See Nos. 000069 and 055558 in § 510.600(c) of this chapter.

(iii) *Related tolerances.* See § 556.510 of this chapter.

(iv) *Conditions of use.* As an intramuscular injection for cattle, sheep, swine, and horses, used as follows:

(a) *Amount.* 3,000 units per pound of body weight (1 milliliter per 100 pounds body weight) daily.¹

(b) *Indications for use.* For the treatment of cattle and sheep for bacterial pneumonia (shipping fever) caused by *Pasteurella multocida*;

data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

swine for erysipelas caused by *Erysipelothrix insidiosa*; and horses for strangles caused by *Streptococcus equi*.¹

(c) *Limitations.* Continue treatment at least 1 day after symptoms disappear (usually 2 or 3 days). Treatment should not exceed 4 consecutive days. Do not exceed 10 milliliters per injection site. Milk that has been taken during treatment and for 72 hours (six milkings) after the latest treatment must not be used for food. Discontinue treatment for the following number of days before slaughter: Cattle—10, sheep—9, and swine—7. Not for use in horses intended for food.

(4)(i) *Sponsor.* See No. 010271 in § 510.600(c) of this chapter.

(ii) See paragraph (c)(3) of this section for specifications, tolerances, and conditions of use of the drug, except discontinue treating cattle 5 days before slaughter and non-ruminating calves 10 days before slaughter.

(5)(i) *Sponsor.* See No. 010515 in § 510.600(c) of this chapter.

(ii) See paragraph (c)(3) of this section for specifications, tolerances, and conditions of use of this drug, except that milk taken during treatment and for 48 hours (four milkings) after the latest treatment shall not be used for food.

[40 FR 13688, Mar. 27, 1975, as amended at 43 FR 32748, July 28, 1978; 43 FR 46529, Oct. 10, 1978; 44 FR 20672, Apr. 6, 1979; 44 FR 49667, Aug. 24, 1979; 46 FR 8468, Jan. 27, 1981; 48 FR 30363, July 1, 1983; 50 FR 2779, Jan. 22, 1985; 50 FR 41490, Oct. 11, 1985; 52 FR 32917, Sept. 1, 1987; 53 FR 11493, Apr. 7, 1988]

§ 540.274c Procaine penicillin G in oil

(a) *Requirements for certification.* The requirements for certification for procaine penicillin G in oil are described under § 440.274a of this chapter, with the following exceptions:

(1) *Standards of identity, strength, quality, and purity.* If it is conspicuously labeled for veterinary use, it may contain furaltadone in accord-

¹ These conditions are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

ance with § 540.874g and is exempt from the potency requirement of § 440.274a(a)(1) of this chapter. It is sterile if it is packaged and labeled solely for udder instillations of cattle and it contains furaltadone. The drug is a suspension in a refined vegetable oil, with or without the addition of one or more suitable and harmless dispersing agents, preservatives, hardening agents, and buffering substances. If the procaine penicillin G in oil is packaged and labeled solely for udder instillations of cattle and is not required to be sterile, the penicillin used is exempt from the requirements of § 440.74a(a)(1) (ii) and (iii) of this chapter.

(2) *Packaging.* If it is labeled solely for udder instillations of cattle it may be packaged in plastic or collapsible tubes which shall be well closed containers as defined by the U.S.P. If it is packaged and labeled solely for veterinary use, it need not meet the requirements for quantity of procaine penicillin in oil in each container, as described in § 440.274a(a)(2) of this chapter.

(3) *Labeling.* When it is packaged for dispensing and intended solely for veterinary use:

(i) If it does not contain adrenocorticotrophic hormone, it shall comply with § 440.274a(a)(3) of this chapter, except in lieu of the statement "Caution: Federal law prohibits dispensing without prescription", each package shall include adequate directions and warnings for the veterinary use of the drug by the laity in all cases except those in which the veterinary prescription statement is required by regulations under this Subchapter E. In those cases, the veterinary prescription statement shall comply with the requirements prescribed by § 201.105 of this chapter. If it is intended for udder instillation in cattle it shall be exempt from the requirements of § 201.100(b)(5) of this chapter.

(ii) If it contains adrenocorticotrophic hormone, it shall comply with § 201.105 of this chapter and with the requirements of § 440.274a(a)(3) of this chapter.

(iii) Each package shall bear on its label and labeling, unless it is intended for udder instillation in cattle, the

statement "Warning—Not for use in animals which are raised for food production".

(4) *Requests for certification; samples.* If the batch of procaine penicillin G in oil is intended solely for udder instillations of cattle and is not required to be sterile, test results for sterility, and pyrogens are not required.

(b) *Tests and methods of assay.* The tests and methods of assay for procaine penicillin in oil are described under § 440.274a of this chapter.

(c) *Conditions of marketing—(1) Specifications.* Sterile procaine penicillin G with aluminum stearate suspension conforms to the standards of identity, strength, quality, and purity prescribed by paragraph (a) of this section. Each milliliter contains 300,000 units of penicillin activity in sesame oil gelled with 2 percent aluminum monostearate.

(2) *Sponsor.* See No. 053501 in § 510.600(c) of this chapter.

(3) *Conditions of use—(i)* It is used as an intramuscular injection in the treatment of infections caused by penicillin-susceptible organisms such as *Streptococci*, *Staphylococci*, and *Corynebacteria*.¹

(ii) It is administered to dogs and cats at 10,000 units per pound of body weight once daily and to horses at 3,000 units per pound of body weight once daily.¹

(iii) The label and labeling shall bear, in addition to the other information required by the act, a statement that the drug is not for use in food-producing animals and a statement that Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

[40 FR 13888, Mar. 27, 1975, as amended at 41 FR 1892, Jan. 13, 1976; 41 FR 11011, Mar. 15, 1976; 50 FR 19922, May 13, 1985; 50 FR 41490, Oct. 11, 1985]

¹ These conditions are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 314.111 of this chapter, but may require bioequivalency and safety information.

§ 540.274d

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§ 540.274d Procaine penicillin in streptomycin sulfate solution; procaine penicillin in dihydrostreptomycin sulfate solution.

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality, and purity.* Procaine penicillin in streptomycin sulfate solution is procaine penicillin G suspended in an aqueous solution of streptomycin sulfate. Procaine penicillin in dihydrostreptomycin sulfate solution is procaine penicillin suspended in an aqueous solution of dihydrostreptomycin sulfate or crystalline dihydrostreptomycin sulfate. Such solution shall contain one or more suitable and harmless buffer substances, preservatives, and suspending or dispersing agents, and it may contain one or more suitable and harmless stabilizing agents, procaine hydrochloride in a concentration not exceeding 2 percent, a suitable antihistaminic, a suitable anticholinergic and cortisone, or a suitable derivative of cortisone. It is so purified that:

(i) Each milliliter shall contain not less than 100,000 units of procaine penicillin and not less than 0.25 gram of streptomycin sulfate or dihydrostreptomycin sulfate, but each immediate container shall contain not less than 300,000 units of procaine penicillin and not less than 0.25 gram of streptomycin sulfate or dihydrostreptomycin sulfate;

(ii) It is sterile;

(iii) It is nonpyrogenic;

(iv) [Reserved]

(v) Its pH is not less than 5.0 and not more than 8.0.

The procaine penicillin used conforms to the requirements prescribed by § 440.74a(a)(1) of this chapter. The streptomycin sulfate used conforms to the requirements prescribed by § 444.70a(a)(1), or § 444.270b(a) of this chapter. The dihydrostreptomycin sulfate used conforms to the requirements prescribed by § 444.10a(a)(1) or § 444.270b(a)(1) of this chapter. Each other substance used, if its name is recognized in the U.S.P. or N.F., conforms to the standards prescribed therefor by such official compendium.

(2) *Packaging.* In all cases the immediate container shall be a tight con-

tainer as defined by the U.S.P., shall be sterile at the time of filling and closing, shall be so sealed that the contents cannot be used without destroying such seal, and shall be of such composition as will not cause any change in the strength, quality, or purity of the contents beyond any limit therefor in applicable standards, except that minor changes so caused which are normal and unavoidable in good packaging, storage, and distribution practice shall be disregarded. In case it is packaged for dispensing, it shall be in immediate containers of transparent glass closed by a substance through which a hypodermic needle may be introduced and withdrawn without removing the closure or destroying its effectiveness, unless it is packaged to contain a single dose. Each such container shall contain not less than 1.0 milliliter, and each shall be filled with a volume in excess of that designated, which excess shall be sufficient to permit the withdrawal and administration of the volume indicated, whether administered in either single or multiple dose.

(3) *Labeling—*(i) *It is packaged for dispensing and it contains an antihistaminic, and anticholinergic, or cortisone or a derivative of cortisone.* In addition to the labeling requirements prescribed by § 201.105 of this chapter (regulations issued under section 502(f) of the act), each package shall bear on the label or labeling, as hereinafter indicated, the following:

(a) On the outside wrapper or container, the statement "Store in refrigerator not above 15° C. (59° F.)."

(b) On the outside wrapper or container and the immediate container, the statement "Expiration date _____", the blank being filled in with the date that is 12 months after the month during which the batch was certified, except that the blank may be filled in with the date that is 18 months, 24 months, or 36 months after the month during which the batch was certified if the person who requests certification has submitted to the Commissioner results of tests and assays showing that after having been stored for such period of time such drug as prepared by him complies with

the standards prescribed by paragraph (a)(1) of this section.

(c) On the label and the labeling, the statement "For use only in cats, dogs and horses; not for use in horses to be slaughtered for human consumption".

(d) After the name procaine penicillin in streptomycin sulfate solution veterinary, or "procaine penicillin in dihydrostreptomycin sulfate solution veterinary", wherever such name appears, the words "with _____", in juxtaposition with such name, the blank being filled in with the established name of the antihistaminic, the anticholinergic, the cortisone, or the derivative of cortisone.

(ii) *It is packaged for dispensing and it does not contain an antihistaminic, an anticholinergic, or cortisone or a derivative of cortisone.* It shall comply with the requirements of paragraph (a)(3)(i) of this section, except:

(a) In lieu of the statement "Caution: Federal law restricts this drug to sale by or on the order of a licensed veterinarian", each package shall include information containing directions and warnings adequate for the veterinary use of the drug by the laity.

(b) If it contains dihydrostreptomycin, an expiration date of 48 months or 60 months may be used if data have been submitted as described in paragraph (a)(3)(i)(b) of this section.

(c) In lieu of the statement required by paragraph (a)(3)(i)(c) of this section, the labeling shall bear the statement "Warning—The use of this drug must be discontinued for 30 days before treated animals are slaughtered for food", and, if the drug is intended for use in animals producing milk for human consumption, the labeling shall also bear the statement required by § 510.106 of this chapter.

(iii) *It is packaged solely for manufacturing use and/or repacking.* Each package shall bear on its outside wrapper or container and the immediate container, the following:

(a) The number of units of procaine penicillin and the number of milligrams or grams of streptomycin sulfate or dihydrostreptomycin sulfate in each milliliter.

(b) The statement "Caution: Federal law prohibits dispensing without prescription".

(c) The statement "For manufacturing use", "For repacking", or "For manufacturing use or repacking".

(d) The information required by paragraphs (a)(3)(i) (a) and (b) of this section.

(4) *Requests for certification; samples.* (i) In addition to complying with the requirements of § 514.50 of this chapter, a person who requests certification of a batch shall submit with his request a statement showing the batch mark, the number of packages of each size in such batch, the number of units of procaine penicillin and the number of milligrams or grams of streptomycin sulfate or dihydrostreptomycin sulfate in each milliliter of the batch, the batch marks and (unless they were previously submitted) the dates on which the latest assays of the procaine penicillin and streptomycin sulfate or dihydrostreptomycin sulfate used in making such batch were completed, the date on which the latest assay of the drug comprising such batch was completed, the quantity of each ingredient used in making the batch, and a statement that each such ingredient conforms to the requirements prescribed therefor by this section.

(ii) Except as otherwise provided by paragraph (a)(4)(v) of this section, such person shall submit in connection with his request results of the tests and assays listed after each of the following made by him on an accurately representative sample of:

(a) The batch: Potency, sterility, pH and, if it does not contain a vegetable oil as a suspending agent, and pyrogens.

(b) The procaine penicillin used in making the batch; potency (pyrogens if it is used in making a batch containing a vegetable oil as a suspending agent), crystallinity, penicillin K content (unless it is procaine penicillin G), and the penicillin G content if it is procaine penicillin G.

(c) The streptomycin sulfate or dihydrostreptomycin sulfate used in making the batch; potency (pyrogens if it is used in making a batch containing a vegetable oil as a suspending agent), depressor substances, strepto-

mycin content if it is dihydrostreptomycin, and crystallinity if it is crystalline dihydrostreptomycin.

(iii) Except as otherwise provided by paragraph (a)(4)(v) of this section, if such batch is packaged for dispensing, such person shall submit in connection with his request, in the quantities hereinafter indicated, accurately representative samples of the following:

(a) The batch:

(1) For all tests except sterility: One immediate container for each 5,000 immediate containers in such batch, but in no case less than 12 immediate containers.

Such samples shall be collected by taking single immediate containers at such intervals throughout the entire time of packaging the batch that the quantities packaged during the intervals are approximately equal.

(2) For sterility testing: 20 immediate containers collected at regular intervals throughout each filling operation when each container contains not less than 600,000 units or not less than 2.0 milliliters, or 40 immediate containers when each contains less than these amounts.

(b) The procaine penicillin used in making the batch; three packages, or 10 packages if it is used to make a batch containing a vegetable oil as a suspending agent, each containing approximately equal portions of not less than 0.5 gram, packaged in accordance with the requirements of § 440.74a(a)(2) of this chapter.

(c) The streptomycin sulfate or dihydrostreptomycin sulfate used in making the batch; six packages, each containing approximately equal portions of not less than 0.5 gram, packaged in accordance with the requirements of § 444.70a(a)(2) of this chapter. If the streptomycin or dihydrostreptomycin used in making the batch is a solution of the drug, the person who requests certification shall dry a sufficient quantity of the solution to meet these sample requirements.

(d) In case of an initial request for certification, each other ingredient used in making the batch; one package of each containing approximately 5 grams.

(iv) If such batch is packaged for repackaging, such person shall submit with his request a sample consisting of:

(a) For all tests except sterility: 12 approximately equal portions of at least 2 milliliters.

(b) For sterility testing: 20 packages, each containing approximately equal portions of at least 4 milliliters.

Each such portion shall be taken from different parts of such batch, and each shall be packaged in a separate container and in accordance with the requirements of paragraph (a)(2) of this section.

(v) No result referred to in paragraphs (a)(4)(ii) (b) and (c) of this section, and no sample referred to in paragraphs (a)(4)(iii) (b) and (c) of this section, is required if such result or sample has been previously submitted.

(b) *Tests and methods of assay*—(1) *Potency*—(i) *Procaine penicillin content*. Proceed as directed in § 440.80a(b)(1) of this chapter, except paragraph (b)(1)(iv) and (ix) of that section. In lieu of the directions in paragraph (b)(4) of this section, place a representative aliquot of the sample in a blending jar, add 1.0 milliliter of polysorbate 80 and sufficient 1 percent phosphate buffer, pH 6.0, to make a total volume of 500 milliliters. Blend 3 to 5 minutes. If the iodometric assay is used, 1 drop of the 1.2 N HCl is added to the blank immediately before the addition of the 0.01 N I. Its content of procaine penicillin is satisfactory if it contains not less than 85 percent of the number of units that it is represented to contain.

(ii) *Streptomycin sulfate content*. Proceed as directed in § 444.70a(b)(1) (x) and (xi) of this chapter.

(iii) *Dihydrostreptomycin sulfate content*. Proceed as directed in § 444.10a(b)(1) of this chapter.

(2) *Sterility*. Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section, except add sufficient penicillinase to the diluting fluid to solubilize the procaine penicillin. Use diluting fluid A; if the product contains lecithin, use diluting fluid D instead. Swirl the flask to completely solubilize the procaine penicillin.

before filtration. If the preparation contains agents that prevent solubilization, proceed as directed in paragraph (c)(2) of that section, using medium B in lieu of medium A.

(3) [Reserved]

(4) *Pyrogens*. Proceed as directed in § 440.250(b)(4).

(5) *pH*. Proceed as directed in § 440.80a(b)(5)(ii) of this chapter, using the undiluted aqueous suspension.

cs. 507, 512(n), 701(f) and (g), 52 Stat. 1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 371(f) and (g))

FR 13658, Mar. 27, 1975, as amended at FR 60569, Dec. 11, 1981; 50 FR 19922, May 13, 1985]

§ 540.281 Crystalline penicillin implantation and injectable dosage forms.

§ 540.281a [Reserved]

§ 540.281b Buffered crystalline penicillin.

(a) *Requirements for certification*. The requirements for certification for buffered crystalline penicillin are deemed under § 440.81 of this chapter. (b) *Tests and methods of assay*. The tests and methods of assay for buffered crystalline penicillin are deemed under § 440.81 of this chapter.

Part C—Ophthalmic and Topical Dosage Forms

§ 540.380 Penicillin ophthalmic and topical dosage forms.

§ 540.380a Penicillin ointment.

(a) *Requirements for certification—Standards of identity, strength, purity, and quality*. Penicillin ointment, is calcium penicillin, crystalline penicillin, procaine penicillin, or penicillin G in a suitable harmless ointment base, with or without a suitable anesthetic. If it is intended for ophthalmic use, it contains crystalline penicillin G and it is sterile. Its moisture content is not more than 1.0 percent. Its potency is not less than 250 units per gram. The ointment conforms to the requirements of § 440.80a(a)(1) of this chapter except the limitation on penicillin

K content and except § 440.80a(a)(1)(i), (ii), (iii) of this chapter, but its potency is not less than 300 units per milligram. The crystalline penicillin G used in making penicillin ophthalmic ointment conforms to the requirements of § 440.80a(a)(1) of this chapter except the limitation on penicillin K content. The procaine penicillin used conforms to the requirements of § 440.74a(a)(1) of this chapter, except paragraph (a)(1)(ii). Each other substance used, if its name is recognized in the U.S.P. or N.F., conforms to the standards prescribed therefor by such official compendium.

(2) *Packaging*. Penicillin ointment, shall be packaged in collapsible tubes, which shall be well-closed containers as defined by the U.S.P. and shall not be larger than the ¼-ounce size if such ointment is represented for ophthalmic use and in no case larger than the 2-ounce size. The composition of the immediate container shall be such as will not cause any change in the strength, quality, or purity of the contents beyond any limit therefor in applicable standards, except that minor changes so caused that are normal and unavoidable in good packaging, storage, and distribution practice shall be disregarded.

(3) *Labeling*. (i) In addition to the labeling requirements prescribed by § 201.105 of this chapter, each package shall bear on its label or labeling, as hereinafter indicated, the following:

(a) An expiration date that conforms to the requirements prescribed by § 432.5(a)(3) of this chapter.

(b) On the outside wrapper or container, the statement "Store in refrigerator not above 15° C. (59° F.)" or "Store below 15° C. (59° F.)", unless the person who requests certification has submitted to the Commissioner results of tests and assays showing that such drug as prepared by him complies with the standards prescribed by paragraph (a)(1) of this section after having been stored at room temperature; but in no case shall such statement be required if it is labeled with an expiration date that is 9 months after the month during which the batch was certified.

(ii) In lieu of the statement "Caution: Federal law restricts this drug to

use by or on the order of a licensed veterinarian," each package shall include information containing directions and warnings adequate for the veterinary use of the drug by the laity.

(4) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The penicillin used in making the batch for potency, moisture, pH, for crystallinity if it is a crystalline salt of penicillin, for heat stability if it is crystalline penicillin or *l*-phenamine penicillin G, for the penicillin G content if it is penicillin G, for the specific rotation if it is *l*-phenamine penicillin G.

(b) The batch for potency and moisture and for sterility if the ointment is intended for ophthalmic use.

(ii) *Samples required:*

(a) The penicillin used in making the batch: Five packages, or in the case of crystalline penicillin, 10 packages, each containing approximately 60 milligrams if it is not procaine penicillin, and approximately 300 milligrams if it is procaine penicillin, packaged in accordance with the requirements of § 440.74a(a)(2) or § 440.80a(a)(2) of this chapter.

(b) *The batch:*

(1) For all tests except sterility: A minimum of five immediate containers.

(2) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay—(1) Potency.* Proceed as directed in § 440.80a(b)(1) of this chapter, except paragraph (ix) of that section, and in lieu of the directions in § 440.80a(b)(1)(iv) of this chapter, prepare the sample by one of the following techniques:

(i) *Extraction.* Place a representative portion of the sample (usually approximately 1 gram, accurately weighed) or the entire contents of a single-dose container in a separatory funnel containing 50 milliliters of peroxide-free ether. If the sample consists of substantially more than 1 gram, use 100 milliliters of peroxide-free ether. Shake the sample and ether until ho-

mogeneous. Add 25 milliliters of 1-percent phosphate buffer, pH 6.0, and shake. If the sample consists of substantially more than 1 gram, use 50 milliliters of buffer. Allow the layers to separate. Remove the buffer layer and repeat the extraction with new portions of buffer at least three times and any additional times necessary to ensure complete extraction of the antibiotic. Combine the extractives and make the proper estimated dilutions with buffer.

(ii) *Blending.* Place an accurately weighed representative portion of the sample (usually approximately 1 gram), or the entire contents of a single-dose container, in a blending jar containing 1.0 milliliter of polysorbate 80 and sufficient 1-percent phosphate buffer, pH 6.0 to give a final volume of 200 milliliters. If the sample consists of substantially more than 1 gram, use sufficient buffer to give a final volume of 500 milliliters. Using a high-speed blender, blend the mixture for 2 minutes and then make the proper estimated dilutions with buffer. Its content of penicillin is satisfactory if it contains not less than 85 percent of the number of units that it is represented to contain.

(2) *Moisture.* Proceed as directed in § 436.500(c) of this chapter, using a weighed sample of approximately 1 gram dissolved in 10 milliliters of a mixture of equal parts of dry chloroform and carbon tetrachloride, but in lieu of calculating the milliliters of Karl Fischer reagent equivalent to 10 milliliters of chloroform, determine the milliliters of reagent equivalent to 10 milliliters of the mixture of chloroform and carbon tetrachloride.

(3) *Sterility.* If the ointment is intended for ophthalmic use, proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(3) of that section.

(Sec. 409, 59 Stat. 463, as amended, 72 Stat. 1775-1788, as amended; sec. 512(i), 82 Stat. 347 (21 U.S.C. 360 b(i)))

[40 FR 13888, Mar. 27, 1975, as amended at 42 FR 19861, Apr. 15, 1977; 50 FR 10922, May 13, 1985]

§ 540.380b Procaine penicillin-neomycin-polymyxin in oil; procaine penicillin-neomycin-polymyxin ointment.

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality, and purity.* Procaine penicillin-neomycin-polymyxin in oil is a suspension of procaine penicillin, neomycin, and polymyxin in refined peanut oil or sesame oil, with or without the addition of one or more suitable and harmless dispersing and suspending agents. Procaine penicillin-neomycin-polymyxin ointment is procaine penicillin, neomycin, and polymyxin in a suitable and harmless ointment base. Each of the drugs may contain a suitable anesthetic, a suitable and harmless preservative, a suitable and harmless salt of cobalt, one or more suitable sulfonamides, and cortisone or a suitable derivative of cortisone. The moisture content of each drug is not more than 10 percent. Each drug contains not less than 25,000 units of procaine penicillin, not less than 17.5 milligrams of neomycin, and not less than 5,000 units of polymyxin per milliliter or per gram. The procaine penicillin used conforms to the requirements of § 40.74a(a)(1) of this chapter, except paragraphs (a)(1)(ii) and (iii) of that section. The neomycin used conforms to the standards prescribed by § 44.42a(a)(1)(i), (v), and (vi) of this chapter. The polymyxin used conforms to the requirements of § 44.170a(a)(1) of this chapter. Each other substance used, if its name is recognized in the U.S.P. or N.F., conforms to the standards prescribed therefor by such official compendium.

(2) *Packaging; labeling; request for certification, samples.* Each drug conforms to all requirements and procedures prescribed for penicillin ointment, veterinary, by § 540.380a(a)(2) except that procaine penicillin-neomycin-polymyxin in oil, veterinary, may be packaged in plastic tubes, (3) and (4), except that:

(i) In addition to the labeling prescribed for penicillin ointment, veterinary, by § 540.380a(a)(3), if they contain one or more of the active ingredients specified in paragraph (a) of this section, each package shall bear on outside wrapper or container and immediate container, after the

name "procaine penicillin-neomycin-polymyxin in oil, veterinary" or "procaine penicillin-neomycin-polymyxin ointment, veterinary", wherever it appears, the words "with _____," the blank being filled in with the established name of each such other ingredient, in juxtaposition with such name.

(ii) In addition to complying with the requirement of § 540.380a(a)(4), a person who requests certification of a batch shall submit with his request a statement showing the batch mark and (unless they were previously submitted) the results and the dates of the latest tests and assays of the neomycin (for potency, moisture, and pH) and polymyxin (for potency) used in making the batch; the number of units of penicillin; the number of milligrams of neomycin, and the number of units of polymyxin per milliliter or per gram. He shall also submit in connection with his requests a sample consisting of five packages each of the neomycin and polymyxin used in making the batch, each package containing approximately equal portions of not less than 0.5 gram.

(b) *Tests and methods of assay—*(1) *Potency—*(i) *Penicillin content.* Proceed as directed in § 540.380a(b)(1). Its content of penicillin is satisfactory if it contains not less than 85 percent of the number of units per milliliter or per gram that it is represented to contain.

(ii) *Neomycin content.* Proceed as directed in § 44.510d(b)(1)(ii) of this chapter, except that sufficient penicillinase is added to the sample under test to inactivate the penicillin. Its content of neomycin is satisfactory if it contains not less than 85 percent of the number of milligrams per milliliter or per gram that it is represented to contain.

(iii) *Polymyxin content.* Proceed as directed in § 436.509(a)(4) of this chapter, except calculate from the quantity of neomycin found (using the method prescribed in paragraph (b)(1)(ii) of this section) the quantity of neomycin that would be present when the sample is diluted to contain 10 units of polymyxin (labeled potency) per milliliter, and prepare the polymyxin standard curve by adding the calculat-

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ed quantity of neomycin to each concentration of polymyxin used for the curve. Use the standard curve to calculate the polymyxin content of the sample. Its content of polymyxin is satisfactory if it contains not less than 85 percent of the number of units per milliliter or gram that it is represented to contain.

(2) *Moisture*. Proceed as directed in § 540.380a(b)(2).

(Sec. 409, 59 Stat. 463, as amended, 72 Stat. 1785-1788)

[40 FR 13688, Mar. 27, 1975, as amended at 50 FR 19922, May 13, 1985]

Subparts D-E—[Reserved]

Subpart F—Intrauterine Dosage Forms

§ 540.680 Ticarcillin.

(a) *Requirements for certification*. See § 440.90a of this chapter.

(b) *Tests and methods of assay*. See § 440.90a of this chapter.

(c) *Conditions of marketing*—(1) *Specifications*. Each vial contains the equivalent of 6 grams of ticarcillin (as ticarcillin disodium) to be reconstituted with 25 milliliters of sterile water for injection or sterile physiological saline, and diluted to desired volume of use.

(2) *Sponsor*. See No. 000029 in § 510.600(c) of this chapter.

(3) *Conditions of use*—(i) *Indications for use*. For intrauterine use in horses for treatment of endometritis caused by beta-hemolytic streptococci.

(ii) *Amount*. 6 grams per day, intrauterine, for 3 consecutive days during estrus.

(iii) *Limitations*. For intrauterine use in horses only. Infuse aseptically. Not for use in horses raised for food production. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[49 FR 34352, Aug. 30, 1984]

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Subpart G—[Reserved]

Subpart H—Intramammary Dosage Forms

§ 540.803 Amoxicillin trihydrate for intramammary infusion.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Amoxicillin trihydrate for intramammary infusion contains sterile amoxicillin trihydrate in a menstruum of refined semisynthetic vegetable oil with a suitable and harmless dispersing agent and preservative. Each 10-milliliter syringe contains amoxicillin trihydrate equivalent to 62.5 milligrams of amoxicillin. Its potency is satisfactory if it contains 90 to 120 percent of the amount of amoxicillin that it is represented to contain. Its moisture content is not more than 1.0 percent. The amoxicillin trihydrate used conforms to the requirements of § 539.3 of this chapter.

(2) *Labeling*. It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter.

(3) *Request for certification samples*. In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) The results of tests and assay on:

(a) The amoxicillin trihydrate used in making the batch for potency, sterility, pyrogens, moisture, pH, amoxicillin content, concordance, identity, and crystallinity.

(b) The batch for potency and moisture.

(ii) *Samples required*:

(a) The amoxicillin trihydrate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch: A minimum of 5 immediate containers.

(b) *Tests and methods of assay*—(1) *Potency*. Proceed as directed for amoxicillin in § 436.105 of this chapter, preparing the sample for assay as follows: Expel the syringe contents into a high-speed glass blender jar containing 489 milliliters of 0.1M potassium phosphate buffer, pH 8.0 (solution 3) and 1 milliliter of polysorbate 80. Blend for 3 to 5 minutes. Further

dilute an aliquot of the blend with solution 3 to the reference concentration of 0.1 microgram of amoxicillin per milliliter.

(2) *Moisture*. Proceed as directed in § 436.201 of this chapter.

(c) *Conditions of marketing*—(1) *Specifications*. The drug conforms to the certification requirements of paragraph (a) of this section.

(2) *Sponsor*. See No. 000029 in § 510.600(c) of this chapter.

(3) *Related tolerances*. See § 556.38 of this chapter.

(4) *Conditions of use*—(i) *Lactating cows*—(a) *Amount*. Each single dose syringe contains 10 milliliters (equivalent to 62.5 milligrams amoxicillin base).

(b) *Indications for use*. For the treatment of subclinical infectious bovine mastitis due to *Streptococcus agalactiae* and *Staphylococcus aureus* (penicillin sensitive).

(c) *Limitations*. Administer after milking. Clean and disinfect the teat. Use one syringe per infected quarter every 12 hours for a maximum of 3 doses. Do not use milk for food purposes if taken from treated animals within 60 hours (5 milkings) after last treatment. Do not slaughter treated animals for food purposes within 12 days after the last treatment. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(ii) [Reserved]

[49 FR 45422, Nov. 16, 1984, as amended at 56 FR 19922, May 13, 1991]

§ 540.814 Benzathine cloxacillin for intramammary infusion.

(a) *Requirements for certification*—

(1) *Standards of identity, strength, quality, and purity*. Benzathine cloxacillin suspension is benzathine cloxacillin in a suitable and harmless oil base. It may contain one or more suitable and harmless preservatives, antioxidants, complexing and suspending agents. Each dose contains benzathine cloxacillin equivalent to 500 milligrams of cloxacillin. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of cloxacillin that it is represented to contain. Its moisture content is not more than 1.0 percent. The benzathine cloxacillin

used conforms to the requirements of § 540.114.

(2) *Labeling*. It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter.

(3) *Request for certification; samples*. In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) The results of tests and assays on:

(a) The benzathine cloxacillin used in making the batch for potency, moisture, pH, identity, and crystallinity.

(b) The batch for potency and moisture.

(ii) *Samples required*:

(a) The benzathine cloxacillin used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch: A minimum of 5 immediate containers.

(b) *Tests and methods of assay*—(1)

Potency. Proceed as directed for cloxacillin in § 436.105 of this chapter using the sodium cloxacillin working standard as the standard of comparison and preparing the sample for assay as follows: Expel the contents of the syringe into a high speed glass blender jar containing sufficient methanol to give a final volume of 500 milliliters. Blend for 3-5 minutes. Immediately dilute an aliquot of this stock solution with solution 1 to the reference concentration of 5.0 micrograms of cloxacillin per milliliter.

(2) *Moisture*. Proceed as directed in § 436.201 of this chapter.

(c) *Conditions of marketing*—(1) *Specifications*. The drug contains benzathine cloxacillin equivalent to 500 milligrams cloxacillin in each dose, and conforms to the certification requirements of paragraph (a) of this section.

(2) *Sponsor*. (i) See code No. 000856 in § 510.600(c) of this chapter for conditions of use as in paragraph (c)(3)(i) of this section.

(ii) See No. 000029 in § 510.600(c) of this chapter, for use as in paragraph (c)(3)(ii) of this section.

(3) *Conditions of use*. (i)(a) The drug is used for treatment of mastitis caused by *Staphylococcus aureus* and *Streptococcus agalactiae* including

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penicillin resistant strains in dairy cows during the dry period.

(b) It is administered aseptically into each infected quarter immediately after last milking or early in dry period.

(c) For use in dry cows only.

(d) Not to be used within 30 days of calving.

(e) Animals infused with this product must not be slaughtered for food use for 30 days after the latest infusion.

(f) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(ii)(a) The drug is used for treatment and prophylaxis of bovine mastitis in nonlactating cows due to *Streptococcus agalactiae* and *Staphylococcus aureus*.

(b) It is administered at one dose in each quarter immediately after last milking.

(c) For use in dry cows only.

(d) Not to be used within 4 weeks (28 days) of calving.

(e) Animals infused with this product must not be slaughtered for food use for 4 weeks (28 days) after the latest infusion.

(f) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13888, Mar. 27, 1975, as amended at 42 FR 1462, Jan. 7, 1977; 46 FR 33030, June 26, 1981; 50 FR 19922, May 13, 1985; 53 FR 27852, July 25, 1988]

§ 540.814a Sterile benzathine cloxacillin for intramammary infusion.

(a) *Requirements for certification*—

(1) *Standards of identity, strength, quality, and purity.* Sterile benzathine cloxacillin suspension veterinary is sterile benzathine cloxacillin in a suitable and harmless oil base. It may contain one or more suitable and harmless preservatives, antioxidants, complexing and suspending agents. Each dose contains benzathine cloxacillin equivalent to 500 milligrams of cloxacillin. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of cloxacillin that it is represented to contain. It is sterile. Its moisture content is not more than 1.0 percent. The benzathine cloxacillin

used conforms to the requirements of § 540.114a.

(2) *Labeling.* It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter.

(3) *Request for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) The results of tests and assays on:

(a) The benzathine cloxacillin used in making the batch for potency, moisture, pH, identity, sterility and crystallinity;

(b) The batch for potency, sterility, and moisture.

(ii) *Samples required:*

(a) The benzathine cloxacillin used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) *The batch:*

(1) For all tests except sterility: A minimum of 5 immediate containers.

(2) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed for cloxacillin in § 436.105 of this chapter using the sodium cloxacillin working standard as the standard of comparison and preparing the sample for assay as follows: Expel the contents of the syringe into a high speed glass blender jar containing sufficient methanol to give a final volume of 500 milliliters. Blend for 3-5 minutes. Immediately dilute an aliquot of the stock solution with solution 1 to the reference concentration of 5.0 micrograms of cloxacillin per milliliter.

(2) *Sterility.* Proceed in accordance with § 436.20 of this chapter using the method described in paragraph (e)(2) of that section, except use medium C in lieu of medium A and medium F in lieu of medium E. During the period of incubation, shake the tubes at least once daily.

(3) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(c) *Conditions of marketing*—(1)(i) *Specifications.* The drug contains benzathine cloxacillin equivalent to 500 milligrams cloxacillin in each 6 milliliters of peanut oil vehicle, and con-

forms to the certification requirements of paragraph (a) of this section.

(ii) *Sponsor.* See No. 053501 in § 510.600(c) of this chapter.

(iii) *Conditions of use.* (a) The drug is used for treatment of mastitis caused by *Staphylococcus aureus* and *Streptococcus agalactiae* in dairy cows at the time of drying-off of the cow.

(b) It is administered aseptically at the rate of 6 milliliters per infected quarter immediately after last milking at the time of drying-off of the cow.

(c) For use in dry cows only.

(d) Not to be used within 30 days of calving.

(e) Milk taken from treated cows prior to 72 hours (6 milkings) after calving must not be used for human food.

(f) Animals infused with this product must not be slaughtered for food from the time of infusion until 72 hours after calving.

(g) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(2)(i) *Specifications.* The drug contains benzathine cloxacillin equivalent to 500 milligrams cloxacillin in each dose, and conforms to the certification requirements of paragraph (a) of this section.

(ii) *Sponsor.* See No. 000029 in § 510.600(c) of this chapter.

(iii) *Conditions of use.* (a) The drug is used for treatment and prophylaxis of bovine mastitis in nonlactating cows due to *Streptococcus agalactiae* and *Staphylococcus aureus*.

(b) It is administered at one dose per infected quarter immediately after last milking.

(c) For use in dry cows only.

(d) Not to be used within 4 weeks (28 days) of calving.

(e) Animals infused with this product must not be slaughtered for food use for 4 weeks (28 days) after the latest infusion.

(f) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13838, Mar. 27, 1975, as amended at 42 FR 1462, Jan. 7, 1977; 50 FR 19922, May 13, 1985; 50 FR 41490, Oct. 11, 1985]

§ 540.815 Sterile sodium cloxacillin for intramammary infusion.

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality, and purity.* Sterile sodium cloxacillin for intramammary infusion contains sterile sodium cloxacillin in a menstruum of refined natural or semi-synthetic vegetable oils with a suitable and harmless dispersing agent. Each milliliter contains sodium cloxacillin equivalent to 20.0 milligrams of cloxacillin. Its potency is satisfactory if it contains 90 to 120 percent of the amount of cloxacillin that it is represented to contain. It is sterile. Its moisture content is not more than 1.0 percent. The sodium cloxacillin used conforms to the requirements of § 539.15 of this chapter.

(2) *Labeling.* It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter.

(3) *Request for certification samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) The results of tests and assay on:

(a) The sodium cloxacillin used in making the batch for potency, sterility, pyrogens, moisture, pH, cloxacillin content, identity, and crystallinity.

(b) The batch for potency, sterility, and moisture.

(ii) *Samples required:*

(a) The sodium cloxacillin used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch: (1) For all tests except sterility: A minimum of 5 immediate containers.

(2) For sterility tests: 20 immediate containers collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay—*(1) *Potency.* Proceed as directed for cloxacillin in § 436.105 of this chapter, preparing the sample for assay as follows: Expel the syringe contents into a high-speed glass blender jar containing 499 milliliters of 1 percent potassium phosphate buffer, pH 6.0 (solution 1) and 1 milliliter of polysorbate 80. Blend for 3 to 5 minutes. Further dilute an aliquot of the blend with solution 1 to the reference concentration

of 5.0 micrograms of cloxacillin per milliliter.

(2) *Sterility*. Proceed in accordance with § 436.20 of this chapter using the method described in paragraph (e)(2) of that section, except use medium C in lieu of medium A and medium F in lieu of medium E. During the period of incubation, shake the tubes at least once daily.

(3) *Moisture*. Proceed as directed in § 436.201 of this chapter.

(c) *Conditions of marketing*—(1) *Specifications*. The drug conforms to the certification requirements of paragraph (a) of this section.

(2) *Sponsor*. See No. 000029 in § 510.600(c) of this chapter.

(3) *Conditions of use*. Lactating cows. (i) *Amount*. 10 milliliters (one dose of 200 milligrams) per infected quarter.

(ii) *Indications for use*. It is used for the treatment of mastitis in lactating cows due to *Streptococcus agalactiae* and *Staphylococcus aureus*, nonpenicillinase producing strains.

(iii) *Limitations*. Administer after milking, cleaning, and disinfecting, and as early as possible after detection. Treatment should be repeated at 12-hour intervals for a total of three doses. Milk taken from treated animals within 48 hours (four milkings) after the latest treatment should not be used for food. Treated animals should not be slaughtered for food purposes within 10 days after the latest treatment period. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[42 FR 64343, Dec. 23, 1977, as amended at 47 FR 14151, Apr. 2, 1982; 50 FR 19922, May 13, 1985]

§ 540.815a Cloxacillin sodium for intramammary infusion.

(a) *Requirements for certification*—

(1) *Standards of identity, strength, quality, and purity*. Cloxacillin sodium for intramammary infusion contains sterile cloxacillin sodium in a menstruum of refined natural or semi-synthetic vegetable oils with a suitable and harmless dispersing agent. Each milliliter contains cloxacillin sodium equivalent 20.0 milligrams of cloxacillin. Its potency is satisfactory if it contains 90 to 120 percent of the amount

of cloxacillin that it is represented to contain. Its moisture content is not more than 1.0 percent. The cloxacillin sodium used conforms to the requirements of § 539.15 of this chapter.

(2) *Labeling*. It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter.

(3) *Request for certification samples*. In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) The results of test and assay on:
(a) The cloxacillin sodium used in making the batch for potency, sterility, pyrogens, moisture, pH, cloxacillin content, identity and crystallinity.

(b) The batch for potency and moisture.

(ii) *Samples required*:

(a) The cloxacillin sodium used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch: A minimum of 5 immediate containers.

(b) *Tests and methods of assay*—(1) *Potency*. Proceed as directed for cloxacillin in § 436.105 of this chapter, preparing the sample for assay as follows: Expel the syringe contents into a high-speed glass blender jar containing 499 milliliters of 1 percent potassium phosphate buffer, pH 6.0 (solution 1) and 1 milliliter of polysorbate 80. Blend for 3 to 5 minutes. Further dilute an aliquot of the blend with solution 1 to the reference concentration of 5.0 micrograms of cloxacillin per milliliter.

(2) *Moisture*. Proceed as directed in § 436.201 of this chapter.

(c) *Conditions of marketing*—(1) *Specifications*. The drug conforms to the certification requirements of paragraph (a) of this section.

(2) *Sponsor*. See No. 000029 in § 510.600(c) of this chapter.

(3) *Conditions for use*. Lactating cows. (i) *Amount*. 10 milliliters (one dose of 200 milligrams) per infected quarter.

(ii) *Indications for use*. It is used for the treatment of mastitis in lactating cows due to *Streptococcus agalactiae* and *Staphylococcus aureus*, nonpenicillinase-producing strains.

(iii) *Limitations.* Administer after milking, cleaning, and disinfecting, and as early as possible after detection. Treatment should be repeated at 12-hour intervals for a total of three doses. Milk taken from treated animals within 48 hours (4 milkings) after the latest treatment should not be used for food. Treated animals should not be slaughtered for food purposes within 10 days after the latest treatment period. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[46 FR 55054, Nov. 13, 1981, as amended at 47 FR 14151, Apr. 2, 1982; 50 FR 19922, May 13, 1985]

§ 540.829 Potassium hetacillin for intramammary infusion.

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality and purity.* Potassium hetacillin for intramammary infusion contains potassium hetacillin in a menstruum of refined peanut oil with a suitable and harmless dispersing agent. It contains in each 10 milliliter syringe an amount of potassium hetacillin equivalent to 62.5 milligrams of ampicillin. Its potency is satisfactory if it contains not less than 90 percent and not more than 120 percent of the number of milligrams of ampicillin that it is represented to contain. It gives a positive identity test for hetacillin. Its moisture content is not more than 1.0 percent. The potassium hetacillin used conforms to the requirements of § 440.29 of this chapter.

(2) *Labeling.* It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter each such request shall contain:

(i) *Results of tests and assays on:*

(a) The potassium hetacillin used in making the batch for potency, moisture, pH, potassium hetacillin content, identity, and crystallinity.

(b) The batch for potency, moisture, and identity.

(ii) *Samples required:*

(a) The potassium hetacillin used in making the batch, 10 packages, each

containing approximately 300 milligrams.

(b) The batch: A minimum of 8 immediate containers.

(b) *Tests and method of assay—*(1) *Potency.* Proceed as directed for ampicillin in § 436.105 of this chapter using the ampicillin working standard as the standard of comparison and preparing the sample for assays as follows: Expel the syringe contents into a high speed glass blending jar containing 1 milliliter of polysorbate 80 and sufficient 0.1M potassium phosphate buffer, pH 8.0 (solution 3) to give a stock solution of convenient concentration. Blend for 3 to 5 minutes. Further dilute an aliquot of the stock solution with solution 3 to the reference concentration of 0.1 microgram of ampicillin per milliliter (estimated).

(2) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(3) [Reserved]

(4) *Hetacillin identity.* Proceed as directed in § 436.305 of this chapter preparing the sample solution as follows: Place 1.0 milliliter of the well-shaken sample into a 50 milliliter volumetric flask. Bring to volume with a 4:1 solution of acetone and 0.1N hydrochloric acid.

(c) *Conditions of marketing—*(1) *Specifications.* The drug is in an oil suspension and conforms to the certification requirements of paragraph (a) of this section.

(2) *Sponsor.* See No. 000856 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) The drug is used for the treatment of acute, chronic, or subclinical bovine mastitis in lactating cows caused by susceptible strains of *Streptococcus agalactiae*, *Streptococcus dysgalactiae*, *Staphylococcus aureus*, and *Escherichia coli*.

(ii) Infuse 10 milliliters (potassium hetacillin equivalent to 62.5 milligrams ampicillin activity) into each infected quarter. Repeat at 24-hour intervals until a maximum of three treatments has been given. If definite improvement is not noted within 48 hours after treatment, the causal organism should be further investigated.

(iii) Milk that has been taken from animals during treatment and for 72 hours (6 milkings) after the latest treatment must not be used for food.

Treated animals must not be slaughtered for food until 10 days after the latest treatment.

(iv) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13888, Mar. 27, 1975, as amended at 40 FR 30941, July 24, 1975; 50 FR 19922, May 13, 1985; 53 FR 27852, July 25, 1988]

§ 540.874 Procaine penicillin G intramammary dosage forms.

§ 540.874a Procaine penicillin G in oil.

(a) *Requirements for certification.* The requirements for certification for procaine penicillin G in oil are described under § 540.274c.

(b) *Tests and methods of assay.* The tests and methods of assay for procaine penicillin G in oil are described under § 540.274c.

(c) *Conditions of marketing—(1) Specifications.* Each dose of the drug contains 100,000 units of procaine penicillin G in a refined vegetable oil.

(2)(i) *Sponsor.* See No. 010515 in § 510.600(c) of this chapter.

(ii) *NAS/NRC status.* The conditions specified in paragraph (c)(2)(iii)(a)(2) of this section have been reviewed by NAS/NRC and are effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(iii) *Conditions of use.* It is used for treatment of bovine mastitis caused by *Streptococcus agalactiae*, *S. dysgalactiae*, and *S. uberis* in lactating cows as follows:

(a) *Three dose regimen.* Administer by intramammary infusion in each infected quarter as follows:

(1) *6-milliliter dose (peanut oil).* Treatment may be repeated at 12-hour intervals. Milk that has been taken from animals during treatment and for 84 hours (7 milkings) after the latest treatment must not be used for food. Animals must not be slaughtered for food during treatment or within 4 days after the latest treatment.

(2) *10-milliliter dose (sesame oil).* Treatment may be repeated at 12-hour intervals. Milk that has been taken from animals during treatment and for 60 hours (5 milkings) after the

latest treatment must not be used for food. Animals must not be slaughtered for food during treatment or within 3 days after the latest treatment.

(b) *Two dose regimen.* This 10-milliliter dose (peanut oil) is administered by intramammary infusion in each infected quarter. Treatment may be repeated at intervals of 12 hours. Milk taken from animals during treatment and for 60 hours (5 milkings) after the latest treatment must not be used for food. Animals must not be slaughtered for food during treatment or within 4 days after latest treatment.

(3)(i) *Sponsor.* See No. 053617 in § 510.600(c) of this chapter.

(ii) *Conditions of use.* It is used for treatment of bovine mastitis caused by *Streptococcus agalactiae*, *S. dysgalactiae*, and *S. uberis* in lactating cows as follows:

(a) This 10-milliliter dose (peanut oil) is administered by intramammary infusion in each infected quarter. Treatment may be repeated at 12-hour intervals for not more than three doses, as indicated by clinical response.

(b) Milk that has been taken from animals during treatment and for 60 hours after the latest treatment must not be used for food.

(c) Animals must not be slaughtered for food during treatment or within 3 days after the latest treatment.

(4)(i) *Sponsor.* See No. 010515 (sesame oil vehicle) and No. 053617 (peanut oil vehicle) in § 510.600(c) of this chapter.

(ii) *NAS/NRC status.* The conditions specified in paragraph (c)(4)(iii) and (iii)(a) of this section have been reviewed by NAS/NRC and are deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(iii) *Conditions of use.* It is used for treatment of bovine mastitis caused by *Streptococcus agalactiae* in dry cows as follows:

(a) *Single dose regimen.* Infuse each infected quarter at time of drying-off with one 10-milliliter dose (sesame oil or peanut oil vehicle).

(b) *Limitations.* Discard all milk for 72 hours (6 milkings) following calving, or later as indicated by the mar-

ketable quality of the milk. Animals must not be slaughtered for food within 14 days postinfusion.

(5)(i) *Sponsor.* See 000010 in § 510.600(c) of this chapter.

(ii) *Conditions of use.* It is used as an aid in the treatment of mastitis caused by *Streptococcus agalactiae*, *S. dysgalactiae*, and *S. uberis* in lactating cows as follows:

(a) *Three dose regimen.* After milking, infuse each infected quarter with a single 10-milliliter syringe (soybean oil vehicle).

(b) *Limitations.* Repeat procedure at 12-hour intervals for not more than 3 doses. Milk that has been taken from animals during treatment and for 60 hours (5 milkings) after the latest treatment must not be used for food. Animals must not be slaughtered for food during treatment or within 3 days after the latest treatment.

[43 FR 8134, Feb. 28, 1978, as amended at 44 FR 47044, Aug. 10, 1979; 44 FR 65977, Nov. 18, 1979; 45 FR 1613, Jan. 8, 1980; 46 FR 43415, Aug. 28, 1981; 50 FR 41135, Oct. 9, 1985; 52 FR 36023, Sept. 25, 1987]

§ 540.874b—540.874c [Reserved]

§ 540.874d Penicillin G procaine-dihydrostreptomycin in soybean oil for intramammary infusion (dry cows).

(a) *Requirements for certification—*

(i) *Standards of identity, strength, quality, and purity.* Penicillin G procaine-dihydrostreptomycin in soybean oil is penicillin G procaine and dihydrostreptomycin sulfate suspended in a soybean oil vehicle. Each 10 milliliters of suspension contains penicillin G procaine equivalent to 200,000 units of penicillin G and dihydrostreptomycin sulfate equivalent to 300 milligrams of dihydrostreptomycin. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of units of penicillin G and the number of grams of dihydrostreptomycin it is represented to contain. Its moisture content is not more than 1.4 percent. The penicillin G procaine used conforms to the standards prescribed by § 440.74a(a)(1) of this chapter, except § 440.74a(a)(1) (ii), (iii), and (iv). The dihydrostreptomycin used conforms to the standards prescribed by § 444.10a(a)(1) of this

chapter, except the standards for sterility, pyrogens, and histamine content.

(2) *Labeling.* It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) The results of tests and assays on:

(a) The penicillin G procaine used in making the batch for potency, moisture, pH, penicillin G content, and crystallinity.

(b) The dihydrostreptomycin sulfate used in making the batch for potency, loss on drying, pH, streptomycin content, and crystallinity, if it is crystalline dihydrostreptomycin.

(c) The batch for penicillin G content, dihydrostreptomycin content, and moisture.

(ii) *Samples required:*

(a) The penicillin G procaine used in making the batch: 5 packages, each containing approximately 500 milligrams.

(b) The dihydrostreptomycin sulfate used in making the batch: 6 packages, each containing approximately 500 milligrams.

(c) The batch: a minimum of 6 immediate containers.

(b) *Tests and methods of assay—(1)*

Potency—(i) Penicillin G content. Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Expel the syringe contents into a high-speed glass blender jar containing 1 milliliter of polysorbate 80 and sufficient 1-percent potassium phosphate buffer, pH 6.0 (solution 1) to give a final volume of 500 milliliters. Blend for 3 to 5 minutes. Further dilute an aliquot of this stock solution with solution 1 to the reference concentration of 1 unit of penicillin G per milliliter (estimated).

(ii) *Dihydrostreptomycin content.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: expel the syringe contents into a high-speed glass blender jar containing 1 milliliter of polysorbate 80 and sufficient 0.1 M potassium phosphate buffer, pH 8.0 (solution 3) to give a final volume of 500 millili-

ters. Blend for 3 to 5 minutes. To an aliquot of this stock solution add sufficient penicillinase to inactivate the penicillin; further dilute with solution 3 to the reference concentration of 1.0 microgram of dihydrostreptomycin per milliliter (estimated). Allow to stand ½ hour at 37° C before filling the cylinders on the plates.

(2) *Moisture*. Proceed as directed in § 436.201 of this chapter.

(c) *Conditions of marketing*—(1) *Specifications*. Each 10-milliliter disposable syringe contains penicillin G procaine equivalent to 200,000 units of penicillin G and 300 milligrams of dihydrostreptomycin base as dihydrostreptomycin sulfate, in a soybean oil vehicle, and conforms to the certification requirements of paragraph (a) of this section.

(2) *Sponsor*. See No. 000010 in § 510.600(c) of this chapter.

(3) *Conditions of use*. (i) For intramammary use for the treatment of subclinical mastitis in dairy cows at the time of drying off. Specifically it should be used against infections caused by *Staphylococcus aureus* and *Streptococcus agalactiae*.

(ii) The drug is administered at the last milking prior to drying off. The drug is infused, 1 syringe into each quarter.

(iii) Not to be used within 6 weeks of calving. For use in dry cows only. Milk taken from cows within 24 hours (2 milkings) after calving must not be used for food. Animals infused with this drug must not be slaughtered for food within 60 days of treatment nor within 24 hours after calving.

[47 FR 43368, Oct. 1, 1982, as amended at 50 FR 19922, May 13, 1985; 50 FR 26197, June 25, 1985]

§ 540.874e Penicillin G procaine-dihydrostreptomycin sulfate for intramammary infusion (dry cows).

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Penicillin G procaine-dihydrostreptomycin sulfate for intramammary infusion (dry cows) is penicillin G procaine and dihydrostreptomycin sulfate suspended in a peanut oil vehicle with aluminum monostearate and hydrogenated peanut oil as gelling and hardening agents. Each 10

milliliters of suspension contains penicillin G procaine equivalent to 1 million units of penicillin G and dihydrostreptomycin sulfate equivalent to 1 gram of dihydrostreptomycin. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of units of penicillin G and the number of grams of dihydrostreptomycin it is represented to contain. Its moisture content is not more than 1.4 percent. The penicillin G procaine used conforms to the standards prescribed by § 440.74a(a)(1) of this chapter, except sterility and pyrogens. The dihydrostreptomycin used conforms to the standards prescribed by § 444.10a(a)(1) of this chapter, except the standards for sterility, pyrogens, and histamine content.

(2) *Labeling*. It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter.

(3) *Requests for certification; samples*. In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) The results of tests and assays on:
(a) The penicillin G procaine used in making the batch for potency, moisture, pH, penicillin G content, and crystallinity.

(b) The dihydrostreptomycin sulfate used in making the batch for potency, loss on drying, pH, streptomycin content, and crystallinity, if it is crystalline dihydrostreptomycin.

(c) The batch for penicillin G content, dihydrostreptomycin content, and moisture.

(ii) *Samples required*:

(a) The penicillin G procaine used in making the batch: 5 packages, each containing approximately 500 milligrams.

(b) The dihydrostreptomycin sulfate used in making the batch: 6 packages, each containing approximately 500 milligrams.

(c) The batch: a minimum of 6 immediate containers.

(b) *Tests and methods of assay*—(1) *Potency*—(i) *Penicillin G content*. Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Expel the syringe contents into a high-speed glass blend-

er jar containing 1 milliliter of polysorbate 80 and sufficient 1-percent potassium phosphate buffer, pH 6.0 (solution 1) to give a final volume of 500 milliliters. Blend for 3 to 5 minutes. Further dilute an aliquot of this stock solution with solution 1 to the reference concentration of 1 unit of penicillin G per milliliter (estimated).

(ii) *Dihydrostreptomycin content.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: expel the syringe contents into a high-speed glass blender jar containing 1 milliliter of polysorbate 80 and sufficient 0.1 M potassium phosphate buffer, pH 8.0 (solution 3) to give a final volume of 500 milliliters. Blend for 3 to 5 minutes. To an aliquot of this stock solution add sufficient penicillinase to inactivate the penicillin; further dilute with solution 3 to the reference concentration of 1.0 microgram of dihydrostreptomycin per milliliter (estimated). Allow to stand ¼ hour at 37° C before filling the cylinders on the plates.

(2) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(c) *Conditions of marketing—(1) Specifications.* Each 10-milliliter disposable syringe contains penicillin G procaine equivalent to 1,000,000 units of penicillin G and 1 gram of dihydrostreptomycin base as dihydrostreptomycin sulfate, in a peanut oil vehicle, and conforms to the certification requirements of paragraph (a) of this section.

(2) *Sponsor.* See No. 033392 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) For intramammary use to reduce the frequency of existing infection and to prevent new infections with *Staphylococcus aureus* in dry cows.

(ii) The drug is administered at the last milking prior to drying off. The drug is infused, 1 syringe into each quarter.

(iii) Not to be used within 6 weeks of freshening. Not for use in lactating cows. Milk taken from animals within 96 hours (8 milkings) after calving must not be used for feed. Animals infused with this drug must not be slaughtered for food within 60 days from the time of infusion nor within 96 hours after calving.

(iv) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13888, Mar. 27, 1975, as amended at 44 FR 55171, Sept. 25, 1979; 50 FR 19922, May 13, 1985; 50 FR 21045, May 22, 1985]

§ 540.874f Procaine penicillin G-novobiocin for intramammary infusion.

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality, and purity.* Procaine penicillin G-novobiocin for intramammary infusion is a suspension of procaine penicillin G and sodium novobiocin in refined vegetable oil with a suitable and harmless suspending agent and preservative. It contains in each 10-milliliter dose 100,000 units of procaine penicillin G and 150 milligrams of novobiocin as sodium novobiocin or 200,000 units of procaine penicillin G and 400 milligrams of novobiocin as sodium novobiocin. Its potency is satisfactory if it is not less than 90 percent and not more than 125 percent of the number of units of penicillin or milligrams of novobiocin that it is represented to contain. Its moisture content is not more than 1.0 percent. The procaine penicillin G used conforms to the requirements of § 440.74a of this chapter, except sterility and pyrogens, and the novobiocin used conforms to the requirements of § 455.51 of this chapter.

(2) *Labeling.* It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The procaine penicillin G used in making the batch for potency percent G content, moisture, pH, and crystallinity.

(b) The sodium novobiocin used in making the batch for potency, loss on drying, pH, specific rotation, identity, and crystallinity.

(c) The batch for potency and moisture.

(ii) *Samples required:*

(a) The procaine penicillin G used in making the batch: 10 packages, each

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containing approximately 300 milligrams.

(b) The sodium novobiocin used in making the batch: 10 packages, each containing approximately 300 milligrams.

(c) The batch: A minimum of 5 immediate containers.

(b) *Tests and methods of assay*—(1) *Potency*. Proceed as directed in § 436.105 of this chapter using test organism 0 in lieu of A to assay for penicillin content, preparing the samples for assay as follows:

(i) *Penicillin content*. Expel the syringe contents into a high speed glass blender jar containing 1 milliliter of polysorbate 80 and sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1) to give a final volume of 500 milliliters. Blend for 3 to 5 minutes. Further dilute an aliquot of this stock solution with solution 1 to the reference concentration of 1 unit of penicillin per milliliter (estimated).

(ii) *Novobiocin content*. Expel the syringe contents into a high speed glass blender jar containing 1 milliliter of polysorbate 80 and sufficient 0.1M potassium phosphate buffer, pH 8.0 (solution 3) to give a final volume of 500 milliliters. Blend for 3 to 5 minutes. To an aliquot of this stock solution, add sufficient penicillinase to inactivate the penicillin; further dilute with 10 percent potassium phosphate buffer, pH 6.0 (solution 6) to the reference concentration of 0.5 microgram of novobiocin per milliliter (estimated). Allow to stand for ½ hour at 37° C before filling the cylinders on the plates.

(2) *Moisture*. Proceed as directed in § 436.201 of this chapter.

(c) *Conditions of marketing*—(1) *Specifications*. The drug contains a suspension of procaine penicillin G, 100,000 units, and novobiocin sodium, equivalent to 150 milligrams of novobiocin, in 10 milliliters of peanut oil vehicle for use in lactating cattle, or procaine penicillin G, 200,000 units, and novobiocin sodium equivalent to 400 milligrams of novobiocin in 10 milliliters of oil for use in dry cows, and conforms to the certification requirements of paragraph (a) of this section.

(2) *Sponsor*. See No. 000009 in § 510.600(c) of this chapter.

(3) *Conditions of use*—(i) *Lactating cows*—(a) *Indications for use*. Use for treating lactating cows for mastitis caused by susceptible strains of *Staphylococcus aureus*, *Streptococcus agalactiae*, *Streptococcus dysgalactiae*, and *Streptococcus uberis*.

(b) *Amount*. Infuse 10 milliliters in each infected quarter after milking. Repeat once after 24 hours.

(c) *Limitations*. For udder instillation in lactating cattle only. Do not milk for at least 6 hours after treatment; thereafter, milk at regular intervals. Milk taken from treated animals within 72 hours (6 milkings) after the latest treatment must not be used for food. Treated animals must not be slaughtered for food for 13 days following the latest treatment. If redness, swelling, or abnormal milk persists, discontinue use and consult a veterinarian.

(ii) *Dry cows*—(a) *Indications for use*. For the treatment of subclinical mastitis caused by susceptible strains of *Staphylococcus aureus* and *Streptococcus agalactiae*.

(b) *Amount*. Infuse 10 milliliters in each quarter at time of drying off.

(c) *Limitations*. For udder instillation in dry cows only. Do not use less than 30 days prior to calving. Milk from treated cows must not be used for food during the first 72 hours after calving. Treated animals must not be slaughtered for food for 30 days following udder infusion.

140 FR 13888, Mar. 27, 1975, as amended at 48 FR 792, Jan. 7, 1983; 50 FR 19922, May 13, 1985]

PART 544—OLIGOSACCHARIDE CERTIFIABLE ANTIBIOTIC DRUGS FOR ANIMAL USE

Subpart A—Oral Dosage Forms

Sec.

544.170 Streptomycin oral dosage forms.

544.170a Streptomycin-polymyxin-bacitracin tablets.

544.170b Streptomycin hydrochloride/streptomycin sulfate oral solution.

544.173 Streptomycin/dihydrostreptomycin oral dosage forms.

544.173a Streptomycin/dihydrostreptomycin tablets.

Sec.

- 544.173b Streptomycin/dihydrostreptomycin syrup; streptomycin/dihydrostreptomycin in gel (streptomycin/dihydrostreptomycin oral suspension); potency.
- 544.173c Streptomycin/dihydrostreptomycin sodium sulfathiazole solution.
- 544.173d Streptomycin/dihydrostreptomycin sulfate oral powder; streptomycin sulfate/dihydrostreptomycin sulfate oral granules; dihydrochloride oral powder/oral granules.
- 544.173e Streptomycin/dihydrostreptomycin-kaolin-pectin-aluminum hydroxide gel powder.

Subpart B—Implantation or Injectable Dosage Forms

- 544.211 Dihydrostreptomycin/streptomycin implantation or injectable dosage forms.
- 544.211a Dihydrostreptomycin/streptomycin sulfates aqueous solution.
- 544.211b Dihydrostreptomycin/streptomycin sulfates.
- 544.274 Streptomycin sulfate/dihydrostreptomycin sulfate/crystalline dihydrostreptomycin sulfate injectable.
- 544.275 Dihydrostreptomycin sulfate injection, sterile.

Subpart C—Ophthalmic and Topical Dosage Forms

- 544.370 Streptomycin ophthalmic and topical dosage forms.
- 544.370a Streptomycin for topical use: streptomycin with (the blank being filled in with the name of the vehicle if a package combination) for topical use.
- 544.370b Streptomycin-erythromycin ointment.
- 544.373 Streptomycin/dihydrostreptomycin ophthalmic and topical dosage forms.
- 544.373a Streptomycin/dihydrostreptomycin ointment.
- 544.373b Streptomycin/dihydrostreptomycin-polymyxin-neomycin ointment.

Subparts D—H [Reserved]

Subpart I—Certain Other Dosage Forms

- 544.973b Streptomycin/dihydrostreptomycin solution for inhalation therapy.

AUTHORITY: Sec. 512, 82 Stat. 343-351 (21 U.S.C. 360b); 21 CFR 5.10, 5.83.

SOURCE: 40 FR 13913, Mar. 27, 1975, unless otherwise noted.

Subpart A—Oral Dosage Forms

§ 544.170 Streptomycin oral dosage forms.

§ 544.170a Streptomycin-polymyxin-bacitracin tablets.

(a) Requirements for certification—

(1) *Standards of identity, strength, quality, and purity.* Streptomycin-polymyxin-bacitracin tablets are tablets composed of streptomycin, polymyxin B, and bacitracin, with or without the addition of one or more suitable and harmless buffer substances, diluents, binders, lubricants, colorings, and flavorings. The potency of each tablet is not less than 250 milligrams of streptomycin, 200,000 units of polymyxin B, and 5,000 units of bacitracin, its loss on drying is not more than 3 percent. Tablets not exceeding 15 millimeters in diameter, or not intended only for preparing solutions, shall disintegrate within 1 hour. The streptomycin used conforms to the standards prescribed therefor by § 444.70a(a)(1) of this chapter, except for sterility, pyrogens, and depressor substances. The polymyxin used conforms to the standards as prescribed by § 448.30(a)(1) of this chapter. The bacitracin used conforms to the standards prescribed therefor by § 448.10(a)(1) of this chapter. Each other substance used, if its name is recognized in the U.S.P. or N.F., conforms to the standards prescribed therefor by such official compendium.

(2) *Packaging.* Unless each tablet is enclosed in a foil or plastic film and such enclosure is a tight container as defined by the U.S.P., except the provision that it shall be capable of tight reclosure, the immediate container shall be a tight container as so defined. The immediate container may also contain a desiccant separated from the tablets by a plug of cotton or other like material. The composition of the immediate container, or of the foil or film enclosure, shall be such as will not cause any change in the strength, quality, or purity of the contents beyond any limit therefor in applicable standards, except that minor changes so caused which are normal and unavoidable in good packaging storage, and distribution practice shall be disregarded.

(3) *Labeling.* In addition to the labeling requirements prescribed by § 510.55 of this chapter, each package shall bear on the outside wrapper or container and the immediate container the statement, "Expiration date ———", the blank being filled in with the date that is 18 months after the month during which the batch was certified.

(4) *Requests for certification; samples.* (i) In addition to complying with the requirements of § 514.50 of this chapter, a person who requests certification of a batch of streptomycin-polymyxin-bacitracin tablets shall submit with his request a statement showing the batch mark, the number of packages of each size in such batch, the batch mark and (unless they were previously submitted) the dates on which the latest assays of the streptomycin, polymyxin, and bacitracin used in making such batch were completed, the potency of each tablet, the quantity of each ingredient used in making the batch, the date on which the latest assay of the drug comprising such batch was completed, and a statement that each ingredient used in making the batch conforms to the requirements prescribed therefor by this section.

(ii) Except as otherwise provided in paragraph (a)(4)(iv) of this section, such person shall submit in connection with his request, results of the tests and assays listed after each of the following, made by him on an accurately representative sample of:

(a) The batch: average potency per tablet, average loss on drying, and if required by paragraph (a)(1) of this section, disintegration time.

(b) The streptomycin used in making the batch: potency, loss on drying, and pH.

(c) The polymyxin used in making the batch: potency.

(d) The bacitracin used in making the batch: potency, loss on drying, and pH.

(iii) Except as otherwise provided by paragraph (a)(4)(iv) of this section, such person shall submit in connection with his request, in the quantities hereinafter indicated, accurately representative samples of the following:

(a) The batch:

(1) For potency and loss on drying: One tablet for each 5,000 tablets in the batch, but in no case less than 30 tablets, collected by taking single tablets throughout the entire time of tableting so that the quantities tableted during the intervals are approximately equal.

(2) For disintegration time: six tablets.

(b) The streptomycin used in making the batch; five packages containing approximately equal portions of not less than 0.5 gram each.

(c) The polymyxin used in making the batch; five packages, each containing approximately equal portions of not less than 0.5 gram.

(d) The bacitracin used in making the batch; six packages, each containing approximately equal portions of not less than 0.5 gram.

(e) In the case of an initial request for certification, each other ingredient used in making the batch; one package of each, containing approximately 5 grams.

(iv) No result referred to in paragraph (a)(4)(iii) (b), (c), and (d) of this section, and no sample referred to in paragraph (a)(4)(iii) (b), (c), and (d) of this section, is required if such result or sample has been previously submitted.

(b) *Tests and methods of assay*—(1) *Potency*—(i) *Streptomycin content.* Using 12 tablets, proceed as directed in § 544.173a(b)(1)(i) of this chapter. Its content of streptomycin is satisfactory if it contains not less than 85 percent of the number of milligrams that it is represented to contain.

(ii) *Polymyxin B content.* Proceed as directed in § 436.105 of this chapter, preparing the sample as follows: Place a representative number of tablets into a high speed glass blender jar containing sufficient 10-percent potassium phosphate buffer, pH 6.0 (solution 6), to give a stock solution of convenient concentration. Blend for 3 to 5 minutes. Remove an aliquot and further dilute with solution 6 to the reference concentration of 10 units of polymyxin B per milliliter (estimated). Its content of polymyxin B is satisfactory if it contains not less than 85 percent of the number of units of polymyxin B it is represented to contain.

(iii) *Bacitracin content.* Proceed as directed in § 436.105 of this chapter, preparing the sample as follows: Place a representative number of tablets into a high speed glass blender jar containing sufficient 1-percent potassium phosphate buffer, pH 6.0 (solution 1) to give a stock solution of convenient concentration. Blend for 3 to 5 minutes. Remove an aliquot and further dilute with solution 1 to the reference concentration of 1 unit of bacitracin per milliliter (estimated). In lieu of the test organisms described in § 436.105 of this chapter, use either test organisms R or V, described in § 436.103 of this chapter. Its content of bacitracin is satisfactory if it is not less than 85 percent of the number of units of bacitracin it is represented to contain.

(2) *Loss on drying.* Proceed as directed in § 436.200(b) of this chapter.

(3) *Disintegration time.* Proceed as directed in § 436.212 of this chapter.

[42 FR 21276, Apr. 26, 1977, as amended at 50 FR 19922, May 13, 1985]

§ 544.170b Streptomycin hydrochloride/streptomycin sulfate oral solution.

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality, and purity.* Streptomycin hydrochloride solution oral and streptomycin sulfate solution oral are aqueous solutions of streptomycin hydrochloride or streptomycin sulfate, with one or more suitable and harmless preservatives and with or without one or more essential vitamin and mineral substances for nutritive purposes. The drug may also contain one or more suitable and harmless buffer substances and stabilizing agents. Its potency is not less than 250 milligrams per milliliter. Its pH is not less than 4 and not more than 7. Each preservative, buffer substance, and stabilizing agent used, if its name is recognized in the U.S.P. or N.F., conforms to the standards prescribed therefor by such official compendium.

(2) *Packaging.* In all cases the immediate container shall be a tight container as defined by the U.S.P. The composition of the immediate container shall be such as will not cause any change in the strength, quality, or purity of the contents beyond any

limit therefor in applicable standards, except that minor changes so caused that are normal and unavoidable in good packaging, storage, and distribution practice shall be disregarded.

(3) *Labeling.* Each package shall bear on the outside wrapper or container and the immediate container:

(i) The batch mark.

(ii) The number of milligrams of streptomycin in each milliliter of the immediate container.

(iii) The statement "Expiration date _____", the blank being filled in with the date that is 12 months after the month during which the batch was certified, except that the blank may be filled in with the date that is 18 months or 24 months after the month during which the batch was certified if the person who requests certification has submitted to the Commissioner results of tests and assays showing that after having been stored for such period of time, such drug as prepared by him complies with the standards prescribed by paragraph (a)(1) of this section.

(iv) The name and quantity of each preservative used.

(v) The statement "For oral veterinary use only".

(vi) If it contains added vitamins or minerals, the name and quantity of each such substance and a statement that such substances are present only for furnishing additional vitamins and minerals while animals are eating less feed.

(vii) If it is intended for use in animals raised for food production, it shall be used in accordance with paragraph (c) of this section.

(4) *Request for certification; samples.* (i) In addition to complying with the requirements of § 514.50 of this chapter, a person who requests certification of a batch shall submit with his request a statement showing the batch mark, the number of packages of each size in the batch, and the number of milligrams of streptomycin per milliliter. Such request shall be accompanied or followed by the results of tests and assays made by him on the batch for potency, and pH.

(ii) Such person shall also submit with his request, in the quantities

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hereinafter indicated, accurately representative samples of the following:

(a) The batch; 1 immediate container for each 5,000 immediate containers in the batch, but in no case less than 5 immediate containers.

(b) In case of an initial request for certification, each other ingredient used in making the batch; 1 package of each containing approximately 5 grams.

(b) *Tests and methods of assay*—(1) *Potency*. Proceed as directed in § 444.70a(b)(1) of this chapter. Its potency is satisfactory if it contains not less than 90 percent of the number of milligrams of streptomycin per milliliter that it is represented to contain.

(2) [Reserved]

(3) *pH*. Proceed as directed in § 444.70a(b)(7) of this chapter.

(c) *Conditions of marketing*—(1) *Specifications*. Complies with the requirements for streptomycin sulfate found in paragraph (a) of this section or § 544.173a(a) or § 544.173d(a).

(2) *Sponsor*. See 033008 in § 510.600(c) of this chapter.

(3) *Special considerations*. The quantities of antibiotic in paragraph (c)(5) of this section refer to the activity of the master standard.

(4) *Related tolerances*. See § 556.610 of this chapter.

(5) *Conditions of use*. It is used as streptomycin sulfate in drinking water as follows:

(i) *Calves*—(a) *Amount per gallon*. 0.5 to 1.5 grams.

(b) *Indications for use*. Treatment of bacterial diarrhea (scours) of calves.

(c) *Limitations*. Administer not more than 5 days; prepare fresh solution daily; withdraw 2 days before slaughter; as sole source of streptomycin.

(ii) *Chickens*—(a) *Amount per gallon*. 0.5 to 1.5 grams.

(b) *Indications for use*. Treatment of chronic respiratory disease (air-sac infection); maintenance of weight gains during periods of stress; treatment of blue comb (nonspecific infectious enteritis).

(c) *Limitations*. Administer not more than 5 days; not for use in laying chickens; prepare fresh solution daily; withdraw 4 days before slaughter; as sole source of streptomycin.

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(iii) *Swine*—(a) *Amount per gallon*. 0.5 to 1.5 grams.

(b) *Indications for use*. Treatment of bacterial enteritis (scours) in swine.

(c) *Limitations*. Administer not more than 4 days; prepare fresh solution daily; as sole source of streptomycin.

[40 FR 13913, Mar. 27, 1975, as amended at 42 FR 21277, Apr. 26, 1977; 50 FR 19922, May 13, 1985; 53 FR 52683, Dec. 29, 1988]

§ 544.173 Streptomycin/dihydrostreptomycin oral dosage forms.

§ 544.173a Streptomycin/dihydrostreptomycin tablets.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Streptomycin tablets and dihydrostreptomycin tablets

are streptomycin or dihydrostreptomycin tablets with or without glucuronolactone, kaolin, or other suitable and harmless absorbent ingredients, pectin, and dried aluminum hydroxide gel, with or without bismuth glycolylarsanilate and one or more suitable sulfonamides, and with or without the addition of one or more suitable and harmless diluents, binders, lubricants, colorings, and flavorings. It may contain chlorhexidine dihydrochloride or vitamin A and/or bismuth subcarbonate. The potency of each tablet is not less than 37.5 milligrams. If it contains chlorhexidine dihydrochloride, each tablet contains 375 milligrams of chlorhexidine dihydrochloride and 37.5 milligrams of dihydrostreptomycin. Its loss on drying is not more than 10 percent. Tablets not exceeding 15 millimeters in diameter, or not intended only for preparing solutions, shall disintegrate within 1 hour. The streptomycin or dihydrostreptomycin used conforms either to the standards prescribed by § 444.70a(a)(1) of this chapter or § 444.10a(a) of this chapter, except the standards for sterility, pyrogens, and depressor substances, or to the standards prescribed by § 539.170(a) of this chapter. Each other substance used, if its name is recognized in the U.S.P. or N.F., conforms to the standards prescribed therefor by such official compendium.

(2) *Packaging.* In all cases the immediate container shall be a well closed container or a tight container as defined by the U.S.P. and it may contain a desiccant separated from the tablets by a plug of cotton or other like material. The composition of the immediate container shall be such as will not cause any change in the strength, quality, or purity of the contents beyond any limit therefor in applicable standards, except that minor changes so caused which are normal and unavoidable in good packaging, storage, and distribution practice shall be disregarded.

(3) *Labeling.* In addition to the labeling requirements prescribed by § 201.105 of this chapter (regulations issued under section 502(f) of the act), each package shall bear on the outside wrapper or container and the immediate container, as hereinafter indicated, the following:

(i) The statement "Expiration date _____", the blank being filled in with the date that is 24 months after the month during which the batch was certified, except that the blank may be filled in with the date that is 36 months or 48 months after the month during which the batch was certified if the person who requests certification has submitted to the Commissioner results of test and assays showing that after having been stored for such period of time such drug as prepared by him complies with the standards prescribed in paragraph (a)(1) of this section.

(ii) If it contains, in addition to streptomycin or dihydrostreptomycin one or more of the other active ingredients specified in paragraph (a)(1) of this section, after the name "streptomycin tablets" or "dihydrostreptomycin tablets", wherever it appears, the words "with _____", the blank being filled in with the established name of each such other ingredient and the words being in juxtaposition with such name.

(iii) In lieu of the statement "Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian", each package shall include information containing directions and warnings adequate for the veterinary use of the drug by the laity.

If it contains bismuth subcarbonate, its label and labeling shall include reference to its use only in cats and dogs.

(iv) If it is intended for use in animals raised for food production, it shall be used in accordance with paragraph (c) of this section, § 544.110(c) or § 544.170b(c).

(4) *Request for certification; samples.* (i) In addition to complying with the requirements of § 514.50 of this chapter, a person who requests certification of a batch of streptomycin or dihydrostreptomycin tablets shall submit with his request a statement showing the batch mark, the number of packages of each size in such batch, the batch mark and (unless it was previously submitted) the date on which the latest assay of the streptomycin or dihydrostreptomycin used in making such batch was completed, the potency of each tablet, the quantity of each ingredient used in making the batch, the date on which the latest assay of the drug comprising such batch was completed, and a statement that each ingredient used in making the batch conforms to the requirements prescribed therefor, if any, by this section.

(ii) Except as otherwise provided in paragraph (a)(4)(iv) of this section, such person shall submit in connection with his request results of the tests and assays listed after each of the following, made by him on an accurately representative sample of:

(a) The batch: Average potency per tablet, average loss on drying, and if required by paragraph (a)(1) of this section, disintegration time.

(b) The streptomycin or dihydrostreptomycin used in making the batch; potency, loss on drying, pH, streptomycin content if it is dihydrostreptomycin, and crystallinity if it is crystalline dihydrostreptomycin sulfate.

(iii) Except as otherwise provided by paragraph (a)(4)(iv) of this section, such person shall submit in connection with his request, in the quantities hereinafter indicated, accurately representative samples of the following:

(a) The batch:

(1) For potency and loss on drying: One tablet for each 5,000 tablets in the batch, but in no case less than 30

tablets, collected by taking single tablets throughout the entire time of tableting so that the quantities tableted during the intervals are approximately equal.

(2) For disintegration time: 6 tablets.

(b) The streptomycin or dihydrostreptomycin used in making the batch; five packages, each containing approximately equal portions of not less than 0.5 gram.

(c) In case of an initial request for certification, each other ingredient used in making the batch; one package of each containing approximately 5 grams.

(iv) No result referred to in paragraph (a)(4)(ii)(b) of this section, and no sample referred to in paragraph (a)(4)(iii)(b) of this section, is required if such result or sample has been previously submitted.

(b) *Tests and methods of assay*—(1) *Potency*—(i) *Streptomycin content*. Using 12 tablets, proceed as directed in § 436.105 of this chapter, preparing the sample as follows: Place the tablets in a glass blending jar containing 500 milliliters of 0.1 M potassium phosphate buffer, pH 8.0. Using a high-speed blender, blend for 3 to 5 minutes and then make the proper estimated dilutions in the buffer solution; except if it is a bolus, add 1 milliliter polysorbate 80 and 499 milliliters of 0.1 M potassium phosphate buffer, pH 8.0, to a glass blending jar, turn on blender, and add three boluses. Blend for 5 minutes and then allow to stand at room temperature for at least 1 hour. Blend again for 5 minutes. Pour contents of blending jar into a beaker, stir with a magnetic stirrer and while stirring remove an aliquot for making the proper estimated dilutions. The average potency of streptomycin tablets is satisfactory if they contain not less than 85 percent of the number of milligrams that they are represented to contain.

(ii) *Dihydrostreptomycin content*. Proceed as directed in paragraph (b)(1)(i) of this section, using the dihydrostreptomycin working standard as a standard of comparison. The average potency of dihydrostreptomycin tablets is satisfactory if it contains not less than 85 percent of the number of milligrams it is represented to contain.

(2) *Loss on drying*. Proceed as directed in § 436.200(b) of this chapter.

(3) *Disintegration time*. Proceed as directed in § 436.212 of this chapter.

(c) *Conditions of marketing*—(i) *Chemical name*. Chlorhexidine dihydrochloride; 1,1'-hexamethylenedi-*p*-chlorophenylbiguanide] dihydrochloride.

(2) *Specifications*. (i) The drug in tablet form conforms to the requirements of § 544.173a(a) of this chapter and in oral suspension to § 544.173b(a) of this chapter.

(ii) Dihydrostreptomycin sulfate is the sulfate salt of the antibiotic substance obtained by hydrogenation of the antibiotic substance produced by the growth of *Streptomyces griseus* or the same antibiotic substance produced by any other means.

(3) *Sponsor*. See No. 000856 in § 510.600(c) of this chapter.

(4) *Special considerations*. The quantities of antibiotic in paragraph (c)(6) of this section refer to the activity of the master standard.

(5) *Related tolerances*. See §§ 556.200 and 556.120 of this chapter.

(6) *Conditions of use*. It is used as dihydrostreptomycin sulfate in tablets or suspension for oral administration to calves as follows:

(i) *Amount*. 150 milligrams of dihydrostreptomycin and 1.5 grams of chlorhexidine dihydrochloride per 100 pounds of body weight per day.

(ii) *Indications for use*. For treatment of bacterial scours in calves.

(iii) *Limitations*. Administer one dose per day for 5 days; withdraw 3 days before slaughter.

(Secs. 507, 512(n), 701(f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 483 as amended, 82 Stat. 350-351 (21 U.S.C. 387, 380b(n), 371(f) and (g)))

[40 FR 13913, Mar. 27, 1975, as amended at 42 FR 21277, Apr. 26, 1977; 46 FR 60501, Dec. 11, 1981; 50 FR 19922, May 13, 1985]

§ 544.173b Streptomycin/dihydrostreptomycin syrup; streptomycin/dihydrostreptomycin in gel (streptomycin/dihydrostreptomycin oral suspension); potency.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Streptomycin

syrup and dihydrostreptomycin syrup are streptomycin or dihydrostreptomycin dissolved in a suitable and harmless diluent that contains one or more suitable and harmless preservatives. Streptomycin in gel and dihydrostreptomycin in gel are streptomycin and dihydrostreptomycin dissolved or suspended in a suitable and harmless gel base that contains a suitable and harmless adsorbent and one or more suitable and harmless preservatives. Each such drug may contain one or more suitable and harmless suspending or dispersing agents, flavorings, pectin, chlorhexidine dihydrochloride, bismuth glycolylarsanilate, bismuth magma, or bismuth subcarbonate suitable mineral salts, procaine hydrochloride, a suitable antispasmodic agent, and one or more suitable sulfonamides. Its potency is not less than 10 milligrams per milliliter; however, if it contains chlorhexidine dihydrochloride, each milliliter contains 12.5 milligrams of chlorhexidine dihydrochloride and 1.25 milligrams of dihydrostreptomycin. The streptomycin conforms to the standard prescribed herefor by § 444.70a(a)(1) of this chapter, except paragraphs (a)(1) (iii), (v), and (vi) of that section. The dihydrostreptomycin used conforms to the standards prescribed therefor by § 444.10a(a) of this chapter respectively, except the standards for sterility, pyrogens, moisture, and depressor substances. Each other substance used, if its name is recognized in the U.S.P. or I.P., conforms to the standards prescribed therefor by such official compendium.

(2) *Packaging.* In all cases the immediate container shall be glass, so closed as to be a tight container as defined by the U.S.P. and of such composition that will not cause any change in the strength, quality, or purity of the contents beyond any limit therefor in applicable standards, except that minor changes so caused which are normal and unavoidable in good packaging, storage, and distribution practice shall be disregarded.

(3) *Labeling.* In addition to the labeling requirements prescribed by § 301.105 of this chapter (regulations issued under section 502(f) of the act), each package shall bear on the outside

wrapper or container and the immediate container, as hereinafter indicated, the following:

(i) The statement "Expiration date _____", the blank being filled in with the date that is 18 months after the month during which the batch was certified, except that the blank may be filled in with the date that is 24 months or 36 months after the month during which the batch was certified if the person who requests certification has submitted to the Commissioner results of tests and assays showing that after having been stored for such period of time such drug as prepared by him complies with the standards prescribed by paragraph (a)(1) of this section.

(ii) If it contains, in addition to streptomycin or dihydrostreptomycin, one or more of the other active ingredients specified in paragraph (a)(1) of this section, after the name "streptomycin sirup", "streptomycin in gel", "dihydrostreptomycin sirup", or "dihydrostreptomycin in gel", wherever such name appears, the words "with _____" (the blank being filled in with the established name of each such other ingredient), in juxtaposition with such name.

(iii) In lieu of the statement, "Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian", each package shall include information containing directions and warnings adequate for the veterinary use of the drug by the laity.

(iv) If it is intended for use in animals raised for food production, it shall be used in accordance with § 544.173a(c).

(4) *Request for certification; samples.* (i) In addition to complying with the requirements of § 514.50 of this chapter, a person who requests certification of a batch shall submit with his request a statement showing the batch mark, the number of packages of each size in such batch, the batch mark and (unless it was previously submitted) the date on which the latest assay of the streptomycin or dihydrostreptomycin used in making the batch was completed, the potency per milliliter of the batch, the quantity of each ingredient used in making the batch, the date on which the latest assay com-

prising such batch was completed, and a statement that each ingredient used in making the batch conforms to the requirements prescribed therefor, if any, by this section.

(ii) Except as otherwise provided in paragraph (a)(4)(iv) of this section, such person shall submit in connection with his request results of the tests and assays listed after each of the following, made by him on an accurately representative sample of:

(a) The batch; average potency per milliliter.

(b) The streptomycin or dihydrostreptomycin used in making the batch; potency, pH, streptomycin content if it is dihydrostreptomycin, and crystallinity if it is crystalline dihydrostreptomycin.

(iii) Except as otherwise provided by paragraph (a)(4)(iv) of this section such person shall submit in connection with his request, in the quantities hereinafter indicated, accurately representative samples of the following:

(a) The batch; one immediate container for each 5,000 immediate containers in the batch, but in no case less than 5 immediate containers, collected by taking single immediate containers at such intervals throughout the entire time of packaging the batch that the quantities packaged during the intervals are approximately equal.

(b) The streptomycin or dihydrostreptomycin used in making the batch; five packages, each containing approximately equal portions of not less than 0.5 gram.

(c) In case of an initial request for certification, each other ingredient used in making the batch; one package of each containing approximately 5 grams.

(iv) No result referred to in paragraph (a)(4)(ii)(b) of this section, and no sample referred to in paragraph (a)(4)(iii)(b) of this section, is required if such result or sample has been previously submitted.

(b) *Tests and methods of assay*—(1) *Streptomycin content.* Proceed as directed in § 446.70a(b)(1) of this chapter. Its potency is satisfactory if it contains not less than 85 percent of the number of milligrams of streptomycin that it is represented to contain.

(2) *Dihydrostreptomycin content.* Using dihydrostreptomycin working standard as a standard of comparison, proceed as directed in § 444.70a(b)(1) of this chapter. Its potency is satisfactory if it contains not less than 85 percent of the number of milligrams of dihydrostreptomycin that it is represented to contain.

(c) *Conditions of marketing.* The conditions of marketing are described under § 544.173a(c).

(Secs. 507, 512(n), 701(f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 337, 380b(n), 371(f) and (g)))

(40 FR 13913, Mar. 27, 1975, as amended at 42 FR 21277, Apr. 26, 1977; 46 FR 60549, Dec. 11, 1981; 50 FR 19922, May 13, 1985)

§ 544.173c Streptomycin/dihydrostreptomycin sodium sulfathiazole solution.

(a) *Requirements for certification*—

(1) *Standards of identity, strength, quality, and purity.* Streptomycin-sodium sulfathiazole solution and dihydrostreptomycin-sodium sulfathiazole solution are streptomycin or dihydrostreptomycin and sodium sulfathiazole dissolved in a suitable and harmless vehicle. Each milliliter contains not less than 35 milligrams of streptomycin or dihydrostreptomycin and not less than 25 milligrams of sodium sulfathiazole. It is sterile. It is nonpyrogenic. It contains no depressor substance. Its pH is not less than 5.0 and not more than 8.0. The streptomycin used conforms to the standards prescribed therefor by § 444.70a(a)(1) of this chapter, except paragraph (a)(1)(vi) of that section. The dihydrostreptomycin used conforms to the standards prescribed therefor by § 444.10a(a) of this chapter, except the standard for moisture. Each other substance used, if its name is recognized in the U.S.P. or N.F., conforms to the standards prescribed therefor by such official compendium.

(2) *Packaging; labeling.* It shall be packaged and labeled in accordance with the requirements of § 510.55 of this chapter; except that in addition to the requirements of § 510.55, each package shall bear on the outside wrapper and container and the immediate container:

- (i) The composition of the vehicle.
- (ii) The number of milligrams of sodium sulfathiazole in each milliliter of the batch.
- (iii) The statement "For veterinary use only".
- (iv) The statement "Warning—Not for use in animals which are raised for food production".

(3) *Requests for certification; samples.* The person who requests certification of a batch shall submit in connection with his request the same information and number of samples for the batch prescribed by § 444.270b(a)(3) of this chapter.

(b) *Tests and methods of assay—(1) Potency.* Proceed as directed in § 444.70b(a)(3) of this chapter, except if it contains dihydrostreptomycin use the dihydrostreptomycin working standard as a standard of comparison. Its content of streptomycin or dihydrostreptomycin is satisfactory if it contains not less than 85 percent of the number of milligrams that it is represented to contain.

(2) *Sterility, pyrogens, depressor substances, streptomycin content if it is dihydrostreptomycin.* Proceed as directed in §§ 444.10a(b)(2) and 444.70a(b)(2), (3), and (5).

(3) [Reserved]

(4) *pH.* Proceed as directed in § 436.202 of this chapter, using the undiluted drug.

(Secs. 507, 512(n), 701(f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371(f) and (g)))

(40 FR 13913, Mar. 27, 1975, as amended at 42 FR 21278, Apr. 26, 1977; 46 FR 60569, Dec. 11, 1981; 50 FR 19922, May 13, 1985)

§ 544.173d Streptomycin/dihydrostreptomycin sulfate oral powder; streptomycin sulfate/dihydrostreptomycin sulfate oral granules; dihydrochloride oral powder/oral granules.

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality, and purity.* Streptomycin sulfate powder oral, streptomycin sulfate granules oral, dihydrostreptomycin sulfate powder oral, dihydrostreptomycin sulfate granules oral, dihydrostreptomycin hydrochloride powder oral, and dihydrostreptomycin hydrochloride granules oral are streptomy-

cin sulfate, dihydrostreptomycin sulfate, or dihydrostreptomycin hydrochloride, with or without one or more suitable and harmless diluents and stabilizing agents, with or without one or more suitable sulfonamides, and with or without one or more essential vitamin and mineral substances for nutritive purposes. Its potency is not less than 3.75 grams per pound. Its loss on drying is not more than 7 percent. The streptomycin or dihydrostreptomycin used conforms to the standards prescribed by § 539.170(a)(1). Each other ingredient used, if its name is recognized in the U.S.P. or N.F., conforms to the standards prescribed therefor by such official compendium.

(2) *Packaging.* In all cases the immediate containers shall be tight containers as defined by the U.S.P. The composition of the immediate containers shall be such as will not cause any change in the strength, quality, or purity of the contents beyond any limit therefor in applicable standards, except that minor changes so caused which are normal and unavoidable in good packaging, storage, and distribution practice shall be disregarded.

(3) *Labeling.* Each package shall bear on its label or labeling as herein after indicated, the following:

(i) On the outside wrapper or container and the immediate container:

(a) The batch mark.

(b) The number of milligrams of streptomycin or dihydrostreptomycin per gram and the number of grams in the immediate container.

(c) If it contains one or more sulfonamides, the name and quantity of each such ingredient.

(d) The statement "Expiration date _____", the blank being filled in with the date that is 12 months (if its potency is less than 150 grams per pound) or 36 months (if its potency is 150 grams or more per pound) after the month during which the batch was certified, except that if the person who requests certification has submitted to the Commissioner results of tests and assays that show that such drug as prepared by him is stable for 24 months, 36 months, 48 months, or 60 months, such date may be used for such drug.

(e) The statement "For oral veterinary use only".

(f) If it contains added vitamins or minerals, the name and quantity of each such substance and a statement that such substances are present only for furnishing additional vitamins and minerals while animals are eating less feed.

(g) If it is intended for use in animals raised for food production, it shall be used in accordance with § 544.170b(c) of this chapter.

(h) The statement "For manufacturing use", "For repackaging", or "For manufacturing use or repackaging", when packaged for repackaging or for use as an ingredient in the manufacture of another drug, as the case may be.

(i) On the label and labeling, if it contains one or more sulfonamides, after the name "streptomycin sulfate powder oral", "streptomycin sulfate granules oral", "dihydrostreptomycin sulfate powder oral", "dihydrostreptomycin sulfate granules oral", "dihydrostreptomycin hydrochloride powder oral", or "dihydrostreptomycin hydrochloride granules oral", wherever such name appears, the words "with sulfonamide(s)", in juxtaposition with such name.

(ii) On the circular or other labeling within or attached to the packaged, adequate directions and warnings for the veterinary use of such drug by the laity. Such circular or other labeling may also bear a statement that a brochure or other printed matter containing information for other veterinary uses of such drug by a veterinarian licensed by law to administer it will be sent to such veterinarian on request.

(4) *Request for certification; samples.* (i) In addition to complying with the requirements of § 514.50 of this chapter, a person who requests certification of a batch shall submit with his request a statement showing the batch mark, the number of packages of each size in such batch, the batch mark and (unless it was previously submitted) the date on which the latest assay of the streptomycin or dihydrostreptomycin used in making such batch was completed, the quantity of each ingredient used in making the batch, the date on which the latest assay of the

drug comprising such batch was completed, and a statement that each other ingredient used conforms to the requirements prescribed therefor, if any, by this section.

(ii) Except as otherwise provided by paragraph (a)(4)(iv) of this section, such person shall submit in connection with his request results of the tests and assays listed after each of the following, made by him on an accurately representative sample of:

(a) The batch; potency and loss on drying.

(b) The streptomycin or dihydrostreptomycin used in making the batch; potency, loss on drying, pH, and streptomycin content if it is dihydrostreptomycin.

(iii) Except as otherwise provided by paragraph (a)(4)(iv) of this section, such person shall submit in connection with his request, in the quantities hereinafter indicated, accurately representative samples of the following:

(a) The batch; one immediate container for each 5,000 immediate containers in the batch, but in no case less than 5 immediate containers, unless each such container is packaged to contain more than 15 grams, in which case the sample shall consist of 15 grams for each 5,000 immediate containers in the batch, but in no case less than five 15-gram portions. Such samples shall be collected by taking single immediate containers or 15-gram portions at such intervals throughout the entire time of packaging the batch that the quantities packaged during the intervals are approximately equal.

(b) The streptomycin or dihydrostreptomycin used in making the batch; 6 packages containing approximately equal portions of not less than 1.0 gram each, packaged in accordance with the requirements of § 539.170(a)(2) of this chapter.

(c) In case of an initial request for certification, the other ingredients used in making the batch; one package of each containing approximately 5 grams.

(iv) No result referred to in paragraph (a)(4)(ii)(b) of this section, and no sample referred to in paragraph (a)(4)(iii)(b) of this section, is required if such result or sample has been previously submitted.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 444.70a(b)(1) of this chapter, except if it contains dihydrostreptomycin use the dihydrostreptomycin working standard as the standard of comparison. Its potency is satisfactory if it contains not less than 90 percent of the number of milligrams of streptomycin or dihydrostreptomycin per gram that it is represented to contain. (2) *Loss on drying.* Using a 1-gram sample, proceed as directed in § 436.200(b) of this chapter.

[40 FR 13913, Mar. 27, 1975, as amended at 42 FR 21278, Apr. 26, 1977; 50 FR 19922, May 13, 1985]

§ 544.173e Streptomycin/dihydrostreptomycin-kaolin-pectin-aluminum hydroxide gel powder.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Streptomycin-kaolin-pectin-aluminum hydroxide gel powder and dihydrostreptomycin-kaolin-pectin-aluminum hydroxide gel powder are streptomycin or dihydrostreptomycin, kaolin, pectin, and dried aluminum hydroxide gel, with or without the addition of one or more suitable and harmless diluents, coloring, and flavorings. Its content of streptomycin or dihydrostreptomycin is not less than 37.5 milligrams per gram of powder. Its loss on drying is not more than 10 percent. The streptomycin used conforms to the standards prescribed therefor by § 444.70a(a)(1) of this chapter, except paragraphs (a)(1) (ii), (iii), and (v) of that section. The dihydrostreptomycin used conforms to the standards prescribed therefor by § 444.10a(a) of this chapter, except the standards for sterility, pyrogens, and depressor substances. Each other substance used, if its name is recognized in the U.S.P. or N.F., conforms to the standards prescribed therefor by such official compendium.

(2) *Packaging.* In all cases the immediate container shall be a tight container as defined by the U.S.P. The composition of the immediate container shall be such as will not cause any change in the strength, quality, or purity of the contents beyond any limits therefor in applicable standards, except that minor changes so caused

which are normal and unavoidable in good packaging, storage, and distribution practice shall be disregarded.

(3) *Labeling.* Each package shall bear, on its label or labeling as hereinafter indicated, the following:

(i) On the outside wrapper or container and the immediate container:

(a) The batch mark.

(b) The number of milligrams of streptomycin or dihydrostreptomycin per gram in the immediate containers.

(c) The quantity of kaolin, pectin, and aluminum hydroxide per gram in the immediate container.

(d) The statement "Expiration date _____", the blank being filled in with the date which is 12 months after the month during which the batch was certified, except that the blank may be filled in with the date which is 24 months, 36 months, or 48 months after the month in which the batch was certified if the person who requests certification has submitted to the Commissioner results of tests and assays showing that after having been stored for such period of time such drug as prepared by him complies with the standards prescribed by paragraph (a)(1) of this section.

(e) The statement "For veterinary use only".

(f) The statement "Warning—Not for use in animals which are raised for food production".

(ii) On the circular or other labeling within or attached to the package, directions and precautions adequate for the use of such powder, including:

(a) Clinical indications.

(b) Dosage and administration.

(c) Contraindications.

(d) Untoward effects that may accompany administration.

If two or more such immediate containers are in such package, the number of circulars or other labeling shall not be less than the number of such containers.

(4) *Request for certification; samples.* (i) In addition to complying with the requirements of § 514.50 of this chapter, a person who requests certification of a batch shall submit with his request a statement showing the batch mark, the number of packages of each size in each such batch, the batch

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mark and (unless it was previously submitted) the date on which the latest assay of the streptomycin or dihydrostreptomycin used in making such batch was completed, the potency per gram of powder, the quantity of each ingredient used in making the batch, the date on which the latest assay of the drug comprising such batch was completed, and a statement that each ingredient used in making the batch conforms to the requirements prescribed therefor, if any, by this section.

(ii) Except as otherwise provided in paragraph (a)(4)(iv) of this section, such person shall submit in connection with his request results of the tests and assays listed after each of the following, made by him on an accurately representative sample of:

(a) The batch; average potency per gram of powder and average loss on drying.

(b) The streptomycin or dihydrostreptomycin used in making the batch; potency, loss on drying, pH, streptomycin content if it is dihydrostreptomycin, and crystallinity if it is crystalline dihydrostreptomycin sulfate.

(iii) Except as otherwise provided by paragraph (a)(4)(iv) of this section, such person shall submit in connection with his request, in the quantities hereinafter indicated, accurately representative samples of the following:

(a) The batch; one immediate container for each 5,000 containers in the batch, but in no case less than 20 such containers, unless each such container is packaged to contain more than 1.0 gram, in which case the sample shall consist of 1.0 gram for each 5,000 immediate containers in the batch, but in no case less than 20 grams. Such samples shall be collected by taking single immediate containers or 1.0-gram portions at such intervals throughout the entire time the containers are being filled that the quantities packaged during the intervals are approximately equal.

(b) The streptomycin or dihydrostreptomycin used in making the batch; 5 packages, in each containing approximately equal portions of not less than 0.5 gram.

(c) In case of an initial request for certification, each other ingredient used in making the batch; one package of each containing approximately 5.0 grams.

(iv) No result referred to in paragraph (a)(4)(ii)(b) of this section, and no sample referred to in paragraph (a)(4)(iii)(b) of this section, is required if such result or sample has been previously submitted.

(b) *Tests and methods of assay*—(i) *Potency*—(i) *Streptomycin content*. Using 3.0 grams of the sample, proceed as directed in § 444.70a(b)(1) of this chapter. Its potency is satisfactory if it contains not less than 85 percent of the number of milligrams of streptomycin it is represented to contain.

(ii) *Dihydrostreptomycin content*. Proceed as directed in paragraph (b)(1)(i) of this section, using the dihydrostreptomycin working standard as a standard of comparison. Its potency is satisfactory if it contains not less than 85 percent of the number of milligrams of dihydrostreptomycin it is represented to contain.

(2) *Loss on drying*. Proceed as directed in § 436.200(b) of this chapter.

(Secs. 507, 512(n), 701(f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371(f) and (g)))

[40 FR 13913, Mar. 27, 1975, as amended at 42 FR 21278, Apr. 26, 1977; 46 FR 60569, Dec. 11, 1981; 50 FR 19922, May 13, 1985]

Subpart B—Implantation or Injectable Dosage Forms

§ 544.211 Dihydrostreptomycin/streptomycin implantation or injectable dosage forms.

§ 544.211a Dihydrostreptomycin/streptomycin sulfates aqueous solution.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Dihydrostreptomycin-streptomycin sulfates solution is an aqueous solution of dihydrostreptomycin-streptomycin sulfates. Such solution conforms to all standards prescribed by § 544.211b(a)(1) for dihydrostreptomycin-streptomycin sulfates, except the limitation on loss on drying, and except that:

(i) It may contain suitable and harmless buffer substances, preservatives, and stabilizing agents. Each other substance used, if its name is recognized in the U.S.P. or N.F., conforms to the standards prescribed therefor by such official compendium.

(ii) Its pH is not less than 5.0 and not more than 7.5.

(2) *Packaging.* It shall be packaged in accordance with the requirements of § 510.45 of this chapter.

(3) *Labeling.* It shall be labeled in accordance with the requirements of § 510.55 of this chapter.

(4) *Request for certification; samples.* In addition to complying with the requirements of § 514.50, a person who requests certification of a batch shall submit in connection with his initial request one package containing approximately 5.0 grams of each other ingredient used in making the batch.

(b) *Tests and methods of assay—(1) Potency.* Proceed as directed in § 444.10a(b)(1) of this chapter. Its total potency is satisfactory if it contains not less than 90 percent of the combined number of milligrams of dihydrostreptomycin and streptomycin than it is represented to contain.

(2) *Content of streptomycin sulfate.* Proceed as directed in § 444.10a(b)(2) of this chapter, making appropriate dilutions so that the aliquot used for the colorimetric measurement contains 5.0 milligrams of streptomycin (estimated), and modify the calculations in accordance with the dilutions made. Its content of streptomycin is satisfactory if it contains not less than 40 percent and not more than 60 percent of the total potency as determined under paragraph (b)(1) of this section.

(3) *Sterility, pyrogens, depressor substances.* Proceed as directed in § 444.70a(b) (2), (3), and (5) of this chapter.

(4) *pH.* Using the undiluted solution, proceed as directed in § 436.202 of this chapter.

(Secs. 507, 512(n), 701(f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371(f) and (g)))

[40 FR 13913, Mar. 27, 1975, as amended at 42 FR 21278, Apr. 26, 1977; 46 FR 60569, Dec. 11, 1981; 50 FR 19922, May 13, 1985]

§ 544.211b Dihydrostreptomycin/streptomycin sulfates.

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality, and purity.* Dihydrostreptomycin-streptomycin sulfates is a mixture of equal parts of dihydrostreptomycin sulfate and streptomycin sulfate. It is so purified and dried that:

- (i) It is sterile.
- (ii) [Reserved]
- (iii) It is nonpyrogenic.
- (iv) It contains no depressor substance.

(v) Its loss on drying is not more than 5 percent.

(vi) Its pH in an aqueous solution containing 0.1 gram of dihydrostreptomycin and 0.1 gram of streptomycin per milliliter is not less than 4.5 and not more than 7.0.

The dihydrostreptomycin sulfate used conforms to the standards prescribed by § 444.10a(a) of this chapter, except the standards for streptomycin content. The streptomycin sulfate used conforms to the standards prescribed by § 444.70a(a)(1) of this chapter.

(2) *Packaging.* It shall be packaged in accordance with the requirements prescribed by § 510.45, except that in case it is packaged for dispensing each immediate container shall contain not less than 0.5 gram of dihydrostreptomycin and 0.5 gram of streptomycin or multiples of each such salt up to and including 5.0 grams of dihydrostreptomycin and 5.0 grams of streptomycin.

(3) *Labeling.* It shall be labeled in accordance with § 510.55 of this chapter, except that each package shall bear on the outside wrapper or container the number of grams of dihydrostreptomycin, the number of grams of streptomycin, and the total number of grams of both salts in the immediate container.

(4) *Request for certification; samples.* (i) In addition to complying with the requirements of § 514.50 of this chapter, a person who requests certification of a batch shall submit with his request a statement showing the batch mark, the number of packages of each size in such batch, the batch marks, and (unless they were previously submitted) the dates on which the latest assays of the dihydrostreptomycin and

streptomycin used in making the batch were completed, the content of dihydrostreptomycin and streptomycin in each container, and the date on which the latest assay of the drug comprising such batch was completed. If such batch or any part thereof is to be packaged with a solvent, such request shall also be accompanied by a statement that such solvent conforms to the requirements described therefor by this section.

(ii) Except as otherwise provided by paragraph (a)(4)(v) of this section, such person shall submit in connection with his request results of the tests and assays listed after each of the following made by him on an accurately representative sample of:

(a) The batch; content of dihydrostreptomycin and streptomycin, sterility, pyrogens, depressor substances, loss on drying, and pH.

(b) The dihydrostreptomycin and streptomycin used in making the batch; potency, and if crystalline dihydrostreptomycin is used, crystallinity.

(iii) Except as otherwise provided by paragraph (a)(4)(v) of this section, such person shall submit in connection with his request, in the quantities hereinafter indicated, accurately representative samples of the following:

(a) The batch:

(1) For all tests except sterility: One immediate container for each 5,000 immediate containers in the batch, but in no case less than six immediate containers.

Such samples shall be collected by taking single immediate containers at such intervals throughout the entire time of packaging the batch that the quantities packaged during the intervals are approximately equal.

(2) For sterility testing: 20 immediate containers collected at regular intervals throughout each filling operation.

(b) The dihydrostreptomycin used in making the batch; three packages, each containing approximately equal portions of not less than 0.5 gram.

(c) The streptomycin used in making the batch; three packages, each containing approximately 0.5 gram.

(iv) If such batch is packaged for repackaging, such person shall submit with

his request a sample consisting of the following:

(a) For all tests except sterility: 4 packages.

(b) For sterility testing: 20 packages.

Each such package shall contain not less than 0.5 gram of dihydrostreptomycin and 0.5 of streptomycin taken from different parts of such batch.

(v) No result referred to in paragraph (a)(4)(ii) of this section, and no sample referred to in paragraph (a)(4)(iii) (b) and (c) of this section, is required if such result or sample has been previously submitted.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 444.10a(b)(1) of this chapter. Its total potency is satisfactory if it contains not less than 90 percent of the combined number of milligrams of dihydrostreptomycin and streptomycin that it is represented to contain.

(2) *Content of streptomycin sulfate.* Proceed as directed in § 444.10a(b)(2) of this chapter, making appropriate dilution so that the aliquot used for the colorimetric measurement contains 5.0 milligrams of streptomycin (estimated) and modify the calculations in accordance with the dilutions made. Its content of streptomycin is satisfactory if it contains not less than 45 percent and not more than 55 percent of the total potency as determined under paragraph (b)(1) of this section.

(3) *Sterility, pyrogens, depressor substances, loss on drying, pH.* Using the total potency of the sample for preparing dilutions and weighings, proceed as directed in § 444.70a(b) (2), (3), (5), (6), and (7) of this chapter.

(Secs. 507, 512(n), 701(f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371(f) and (g)))

[40 FR 13913, Mar. 27, 1975, as amended at 42 FR 21278, Apr. 26, 1977; 46 FR 60569, Dec. 11, 1981; 50 FR 19922, May 13, 1985]

§ 544.274 Streptomycin sulfate/dihydrostreptomycin sulfate/crystalline dihydrostreptomycin sulfate injectable.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Streptomycin sulfate injection is an aqueous solution of streptomycin sulfate. Dihydrostrepto-

mycin sulfate injection is an aqueous solution of dihydrostreptomycin sulfate or crystalline dihydrostreptomycin sulfate. Such solution conforms to all standards prescribed by § 444.70a(a) of this chapter for streptomycin sulfate or § 444.10a(a) of this chapter for dihydrostreptomycin sulfate or crystalline dihydrostreptomycin sulfate, except:

(i) The limitation on moisture content does not apply.

(ii) The depressor substances test may be omitted if it has been performed on streptomycin sulfate, dihydrostreptomycin sulfate, or crystalline dihydrostreptomycin sulfate used in preparing the solution.

(iii) It contains one or more suitable and harmless preservatives.

(iv) Its pH is not less than 5.0 and not more than 8.0.

(v) It may contain one or more suitable and harmless buffer substances and stabilizing agents.

(2) *Packaging.* In all cases the immediate container shall be a tight container as defined by the U.S.P., shall be sterile at the time of filling and closing, shall be so sealed that the contents cannot be used without destroying the seal, and shall be of such composition as will not cause any change in the strength, quality, or purity of the contents beyond any limit therefor in applicable standards, except that minor changes so caused which are normal and unavoidable in good packaging, storage, and distribution practice shall be disregarded.

(3) *Labeling.*—(i) It shall be labeled in accordance with the requirements prescribed by § 201.105 of this chapter and each package shall include information containing directions and warnings adequate for the veterinary use of the drug by the laity in lieu of the statement "Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian" (as provided in § 201.105(b)(1) of this chapter) unless such statement is required by regulations issued under section 512(i) of the act.

(ii) Its labeling shall bear any additional information required for the drug by specific regulations.

(iii) On the outside wrapper or container and the immediate container,

the statement "Expiration date _____", the blank being filled in with the date that is 12 months after the month during which the batch was certified except that the blank may be filled in with the date that is 18 months, 24 months, 36 months, 48 months, or 60 months after the month during which the batch was certified if the person who requests certification has submitted to the Commissioner results of tests and assays showing that after having been stored for such period such drug as prepared by him complies with the standards prescribed by paragraph (a)(1) of this section.

(iv) On the outside wrapper or container the statement "Store in refrigerator not above 15° C. (59° F.)" or "Store below 15° C. (59° F.)" unless the person who requests certification has submitted to the Commissioner results of tests and assays showing that such drug as prepared by him complies with the standards prescribed by paragraph (a)(1) of this section after having been stored at room temperature.

(v) The statement "Warning—The use of this drug must be discontinued for 30 days before treated animals are slaughtered for food." If the drug is intended for use in animals producing milk for human consumption, the labeling shall also bear the statement "Milk that has been taken from animals during treatment and for _____ hours (_____ milkings) after the latest treatment must not be used for food," the blanks being filled with the figures 96 and 8 respectively, unless the sponsor of the drug has submitted the results of tests and assays demonstrating that residues of the drug in milk from treated animals persist for a shorter period of time and the shorter period is authorized by the Commissioner.

(4) *Request for certification, check tests and assays; samples.* (i) In addition to complying with the requirements of § 514.50 of this chapter, a person who requests certification of a batch shall submit with his request a statement showing the batch mark, the number of packages of each size in the batch, the number of milligrams or grams dissolved in each of such packages, the date on which the latest assay of the drug comprising such

batch was completed, and if it is crystalline dihydrostreptomycin sulfate injection, the batch mark and (unless it was previously submitted) the date on which the latest assay of the crystalline dihydrostreptomycin sulfate used in making such batch was completed.

(ii) Except as otherwise provided by paragraph (a)(4)(iv) of this section, such person shall submit in connection with his request results of the tests and assays listed after each of the following, made by him on an accurately representative sample of:

(a) The batch; potency, sterility, pyrogens, depressor substances (except that the result of this test performed on the streptomycin sulfate, dihydrostreptomycin sulfate, or crystalline dihydrostreptomycin sulfate used in making the batch may be submitted instead), pH, and streptomycin content, if it is dihydrostreptomycin sulfate or crystalline dihydrostreptomycin sulfate.

(b) The streptomycin sulfate or dihydrostreptomycin sulfate used in making the batch; potency on dry basis and crystallinity if it is crystalline dihydrostreptomycin sulfate.

(iii) Except as otherwise provided by paragraph (a)(4)(iv) of this section such person shall submit in connection with his request, in the quantities hereinafter indicated, accurately representative samples of the following:

(a) The batch, if packaged¹ for dispensing:

(1) For all tests except sterility: One immediate container for each 5,000 immediate containers in such batch; but in no case less than five immediate containers.

Such samples shall be collected by taking single immediate containers at such intervals throughout the entire time of packaging the batch that the quantities packaged during the intervals are approximately equal.

(2) For sterility testing: 20 immediate containers collected at regular intervals throughout each filling operation.

(b) The batch, if packaged for use in the manufacture of another drug:

(1) For all tests except sterility: Five packages.

(2) For sterility testing: 20 packages.

Each such package shall contain approximately 2 milliliters, taken from a different part of such batch, and each shall be packaged in accordance with the requirements of paragraph (a)(2) of this section.

(c) The streptomycin or dihydrostreptomycin used in making the batch; one immediate container, unless it is crystalline dihydrostreptomycin, in which case the sample shall consist of three immediate containers. Each immediate container shall contain approximately 0.5 gram of the dried drug. If the streptomycin or dihydrostreptomycin used in making the batch is a solution of the drug, the person who requests certification shall dry a sufficient quantity of such solution for potency testing on the dry basis.

(d) In case of an initial request for certification, each other ingredient used in making the batch; one package of each containing approximately 5 grams.

(iv) No result referred to in paragraph (a)(4)(ii)(b) of this section, and no sample referred to in paragraph (a)(4)(iii)(c) of this section is required if such result or sample has been previously submitted.

(v) In connection with contemplated requests for certification of repackaged batches or batches of another drug in the manufacture of which it is to be used, the manufacturer of the batch which is to be so repacked or used may request the Commissioner to make check tests and assays on a sample of such batch, taken as prescribed by paragraph (a)(4)(iii)(b) of this section. From the information required by paragraph (a)(4)(ii)(a) of this section may be omitted results of tests and assays not required for the batch when used in such other drug. The Commissioner shall report to such manufacturer results of such check tests and assays as are so requested.

(b) *Tests and methods of assay.* (1) If it is streptomycin sulfate injection, proceed as directed in § 444.70a(b) of this chapter.

(2) If it is dihydrostreptomycin sulfate injection or crystalline dihydrostreptomycin sulfate injection, proceed as directed in § 444.10a(b) of this

chapter, except that the depressor substances test may be omitted if it is performed on the dihydrostreptomycin sulfate or crystalline dihydrostreptomycin sulfate used in preparing the injection, and except that in lieu of the directions in § 444.10a(b)(2) of this chapter determine the streptomycin content as follows:

(i) *Preparation of standard.* Prepare a standard aqueous solution of the Food and Drug Administration streptomycin working standard containing 0.25 milligram of streptomycin base per milliliter. Transfer 1.0, 1.5, and 2.0 milliliter aliquots to test tubes (approximately 16 millimeters $\times$ 150 millimeters). Add 1.0, 0.5, and 0 milliliter of distilled water to give a 2.0-milliliter volume.

(ii) *Preparation of sample.* Dilute 1.0 milliliter of the dihydrostreptomycin sulfate solution to be tested (containing 250 to 500 milligrams of dihydrostreptomycin) to 25.0 milliliters in a volumetric flask. Transfer 2.0 milliliters to a test tube.

(iii) *Blank.* Use 2.0 milliliters of distilled water.

(iv) *Procedure.* To each tube containing 2.0 milliliters, add, in turn, 8.0 milliliters of 0.1N NaOH (freshly prepared from 1N NaOH), mix thoroughly, and immediately determine the optical density at 325 m μ in a suitable spectrophotometer. Set the spectrophotometer at 100-percent light transmission for the blank similarly treated. Return the solution to the test tube, heat in a boiling water bath for 10 minutes, cool in an ice bath for 3 minutes, and allow to come to room temperature. Determine the optical density at 325 m μ . The difference in reading before and after heating is the optical density of the aliquot. Prepare a standard curve. The concentration of streptomycin in the sample solution obtained directly from the standard curve times 1,250, divided by the number of milligrams of dihydrostreptomycin in the original dihydrostreptomycin solution, equals the percent of streptomycin.

(Secs. 507, 512(n), 701(f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371(f) and (g)))

[40 FR 13913, Mar. 27, 1975, as amended at 42 FR 21279, Apr. 26, 1977; 46 FR 60569, Dec. 11, 1981; 47 FR 24291, June 4, 1982; 50 FR 19922, May 13, 1985]

§ 544.275 Dihydrostreptomycin sulfate injection, sterile.

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality, and purity.* Dihydrostreptomycin sulfate injection, sterile, is an aqueous solution of dihydrostreptomycin sulfate. It contains one or more suitable and harmless preservatives and buffer substances. Each milliliter contains dihydrostreptomycin sulfate equivalent to 500 milligrams of dihydrostreptomycin. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the labeled amount of dihydrostreptomycin. It is sterile. It is nonpyrogenic. It contains no depressor substances. This test may be omitted if the dihydrostreptomycin sulfate used in making the batch was tested. Its pH is not less than 5.0 and not more than 8.0. The dihydrostreptomycin sulfate used in making the batch conforms to the requirements of § 444.10a(a) of this chapter.

(2) *Labeling.* It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) The results of tests and assays on:

(a) The dihydrostreptomycin sulfate used in making the batch for potency, depressor substances, loss on drying, pH, streptomycin content, and identity.

(b) The batch for potency, sterility, pyrogens, depressor substances, except that if the dihydrostreptomycin sulfate used has been tested for depressor substances this test may be omitted, and pH.

(ii) *Samples required:*

(a) The dihydrostreptomycin sulfate used in making the batch: 10 packages, each containing approximately 500 milligrams.

(b) The batch: (1) For all tests except sterility: A minimum of 5 immediate containers.

(2) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Using a suitable hypodermic needle and syringe, remove an accurately measured representative portion of the sample and dilute with sterile distilled water to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution to the reference concentration of 30 micrograms of dihydrostreptomycin per milliliter (estimated).

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Pyrogens.* Proceed as directed in § 436.32 of this chapter, using a solution containing 10 milligrams of dihydrostreptomycin per milliliter.

(4) *Depressor substances.* Proceed as directed in § 436.35 of this chapter.

(5) *pH.* Proceed as directed in § 436.202 of this chapter, using the undiluted solution.

(c) *Conditions of marketing*—(1) *Specifications.* The product conforms to the requirements of paragraph (a) of this section.

(2) *Sponsor.* See Nos. 000069 and 010719 in § 510.600(c) of this chapter for use as in paragraphs (c)(4) (i), (ii), and (iii)(a) of this section; see No. 010271 for use as in paragraphs (c)(4) (i), (ii), and (iii)(b) of this section.

(3) *NAS/NRC status.* These conditions are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter but may require bioequivalency and safety information.

(4) *Conditions of use*—(i) *Amount.* 5 milligrams per pound of body weight every 12 hours.

(ii) *Indications for use.* Treatment of leptospirosis in dogs and horses due to *Leptospira canicola*, *L. Icterohemorrhagiae*, and *L. pomona*; in cattle due to *L. pomona*; and in swine due to *L. pomona* and *L. grippotyphosa*.

(iii) *Limitations.* (a) Administer by deep intramuscular injection only.

Treatment should be continued for 3 to 5 days or until the urine is free of leptospira for at least 72 hours as measured by darkfield microscopic examination. Treatment with subtherapeutic dosages, excessive duration of therapy, or inappropriate use of this antibiotic may lead to the emergence of streptomycin or dihydrostreptomycin resistant organisms. The use of this drug must be discontinued for 30 days before treated animals are slaughtered for food. The drug is not for use in animals producing milk because use of the drug will result in contamination of the milk. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(b) Administer by deep intramuscular injection only. Treatment should be continued for 3 to 5 days or until the urine is free of leptospira for at least 72 hours as measured by darkfield microscopic examination. Treatment with subtherapeutic dosages, excessive duration of therapy, or inappropriate use of this antibiotic may lead to the emergence of streptomycin or dihydrostreptomycin resistant organisms. The use of this drug must be discontinued for 30 days before treated animals are slaughtered for food. Milk taken from animals during treatment and for 48 hours (4 milkings) after latest treatment must not be used for food. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[47 FR 24291, June 4, 1982, as amended at 50 FR 5386, Feb. 8, 1985; 50 FR 19922, May 13, 1985]

Subpart C—Ophthalmic and Topical Dosage Forms

§ 544.370 Streptomycin ophthalmic and topical dosage forms.

§ 544.370a Streptomycin for topical use: streptomycin with (the blank being filled in with the name of the vehicle if a package combination) for topical use.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Streptomycin for topical use conforms to all the requirements prescribed by § 444.70a(a)(1) of this chapter for streptomycin, and may be packaged in combination with

a container of a suitable and harmless vehicle.

(2) *Packaging.* The immediate container of streptomycin for topical use shall be of colorless transparent glass so closed as to be a tight container as defined by the U.S.P., shall be sterile at the time of filling and closing, shall be so sealed that its contents cannot be used without destroying such seal, and shall be of such composition as will not cause any change in the strength, quality, or purity of the contents beyond any limit therefor in applicable standards, except that minor changes so caused which are normal and unavoidable in good packaging, storage, and distribution practice shall be disregarded. Each such container shall contain not less than 20 milligrams.

(3) *Labeling.* In addition to the labeling requirements prescribed by § 201.105 of this chapter (regulations issued under section 502(f) of the act), each package shall bear on its outside label or labeling, as hereinafter indicated, the following:

(i) On the outside wrapper or container and the immediate container, the statement, "Expiration date _____" the blank being filled in with the date that is 48 months after the month during which the batch was certified.

(ii) If it is a packaged combination, on the immediate container of the vehicle in the combination, a statement giving the method of dissolving the streptomycin in the vehicle and the statement "The solution may be stored at room temperature for 1 week without significant loss of potency".

(4) *Requests for certification; samples.* (i) In addition to complying with the requirements of § 514.50 of this chapter, a person who requests certification of a batch of streptomycin for topical use shall submit with his request a statement showing the batch mark, the number of packages of each size in each batch, the number of milligrams in each package, and (unless it was previously submitted) the date on which the latest assay of the drug comprising the batch was completed. Such request shall be accompanied or followed by the results of tests and assays made by him on the batch for

potency, sterility, pyrogens, depressor substances, loss on drying, and pH. If such batch, or any part thereof, is to be packaged with a vehicle, such request shall be accompanied by a statement that such vehicle conforms to the requirements prescribed therefor by the section.

(ii) Such person shall submit in connection with his request an accurately representative sample of the batch, consisting of the following:

(a) For all tests except sterility: One immediate container for each 5,000 immediate containers in such batch; but in no case less than 50 immediate containers.

Such samples shall be collected by taking single immediate containers, before or after labeling, at such intervals throughout the entire time of packaging the batch so that the quantities packaged during the intervals are approximately equal.

(b) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(iii) In case of an initial request for the certification of a batch of streptomycin for topical use which is to be packaged in combination with a container of a vehicle, or when any change is made in the composition of such vehicle, such person shall submit in connection with his request five packages of the vehicle included in the combination.

(b) *Tests and methods of assay—(1) Potency.* Proceed as directed in § 444.70a(b)(1) of this chapter. The potency of streptomycin for topical use is satisfactory if the immediate containers are represented to contain:

(i) Less than 500 milligrams and contain 85 percent or more of the number of milligrams so represented;

(ii) More than 500 milligrams and contain 90 percent or more of the number of milligrams so represented.

(2) *Sterility, pyrogens, depressor substances, loss on drying, pH.* Proceed as directed in § 444.70a(b)(2), (3), and (5) through (7).

(Secs. 507, 512(n), 701(f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371(f) and (g)))

§ 544.370b

[42 FR 21279, Apr. 26, 1977, as amended at 46 FR 60569, Dec. 11, 1981; 50 FR 19922, May 13, 1985]

§ 544.370b Streptomycin-erythromycin ointment.

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality, and purity.* Streptomycin-erythromycin ointment is streptomycin and erythromycin in a suitable and harmless ointment base, with or without one or more suitable sulfonamides and with or without suitable and harmless dispensing and suspending agents. Its moisture content is not more than 1.0 percent. It contains per gram not less than 3 milligrams of streptomycin and not less than 5 milligrams of erythromycin. The streptomycin used conforms to the requirements of § 444.70a(a)(1) of this chapter, except for sterility, pyrogens, and depressor substances. The erythromycin used conforms to the standards prescribed by § 452.10(a)(1), except for residue on ignition, heavy metals, and crystallinity. Each other substance used, if its name is recognized in the U.S.P. or N.F., conforms to the standards prescribed therefor by such official compendium.

(2) *Packaging.* Streptomycin-erythromycin ointment shall be packaged in collapsible tubes which shall be well-closed containers as defined by the U.S.P. The composition of the immediate container shall be such as will not cause any change in the strength, quality, or purity of the contents beyond any limit therefor in applicable standards, except that minor changes so caused that are normal and unavoidable in good packaging, storage, and distribution practice shall be disregarded.

(3) *Labeling.* Each package shall bear on its label or labeling, as herein-after indicated, the following:

(i) On the outside wrapper or container and the immediate container:

(a) The batch mark.

(b) The number of milligrams of streptomycin and the number of milligrams of erythromycin in each gram or milliliter of the batch.

(c) If it contains one or more sulfonamides, the name and quantity of each

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such ingredient in each gram or milliliter of the batch.

(d) The statement "For veterinary use only".

(e) The statement "Expiration date—", the blank being filled in with the date that is 12 months after the month during which the batch was certified except that the blank may be filled in with the date which is 18 months, 24 months, or 36 months after the month during which the batch was certified if the person who requests certification has submitted to the Commissioner results of tests and assay showing that after having been stored for such period of time, such drug as prepared by him complies with the standards prescribed by paragraph (a)(1) of this section: *Provided, however,* That such expiration date may be omitted from the immediate container if it contains a single dose and it is packaged in an individual wrapper or container.

(ii) On the label and labeling, if it contains one or more sulfonamides, after the name "streptomycin-erythromycin ointment", wherever it appears the words "with sulfonamide(s)", in juxtaposition with such name.

(iii) On the circular or other labeling within or attached to the package, adequate directions and warnings for the veterinary use of such drug by the laity. Such circular or other labeling may also bear a statement that a brochure or other printed matter containing information for other veterinary uses of such drug by a veterinarian licensed by law to administer it will be sent to such veterinarian on request.

(4) *Requests for certification; samples.* (i) In addition to complying with the requirements of § 514.50 of this chapter, a person who requests certification of a batch shall submit with his request a statement showing the batch mark and (unless they were previously submitted) the dates on which the latest assays of the streptomycin and erythromycin used in making such batch were completed, the quantity of each ingredient used in making the batch, the date on which the latest assay of the drug comprising such batch was completed, and a statement that each ingredient used in making the batch conforms to the require-

ments prescribed therefor by this section.

(ii) Except as otherwise provided by paragraph (a)(4)(iv) of this section, such person shall submit in connection with his request results of the tests and assays listed after each of the following, made by him on an accurately representative sample of:

(a) The batch: Potency and moisture.

(b) The streptomycin and erythromycin used in making the batch: Potency, pH, loss on drying, and color-identity test, if it is erythromycin.

(iii) Except as otherwise provided by paragraph (a)(4)(iv) of this section, such person shall submit in connection with his request, in the quantities hereinafter indicated, accurately representative samples of the following:

(a) The batch: 1 immediate container for each 5,000 immediate containers in the batch, but in no case less than 6 immediate containers, collected by taking single immediate containers at such intervals throughout the entire time of packaging the batch that the quantities packaged during the intervals are approximately equal.

(b) The streptomycin used in making the batch: six packages, each containing approximately equal portions of not less than 0.5 gram.

(c) The erythromycin used in making the batch: 5 packages, each containing approximately equal portions of not less than 0.5 gram.

(d) In case of an initial request for certification, the ingredients used in making the ointment base of the batch: 1 package of each, containing approximately 200 grams, except for the suspending or dispersing agents and sulfonamides used, in which case the sample shall consist of approximately 5 grams.

(iv) No result referred to in paragraph (a)(4)(ii)(b) of this section, and no samples referred to in paragraph (a)(4)(iii)(b) and (c) of this section, is required if such result or samples have been previously submitted.

(b) *Tests and methods of assay*—(1) *Potency*—(i) *Streptomycin content*. Proceed as directed in § 436.105 of this chapter, except prepare the sample as follows: Place a representative quantity of the ointment (usually an entire

container) in a blending jar containing approximately 225 milliliters of chloroform. Using a high-speed blender, blend the mixture for 3 minutes. Transfer the blended material to a large Buchner funnel (at least 10 centimeters in diameter) fitted with a highly retentive filter paper and attached to a vacuum line. Apply vacuum long enough to ensure removal of chloroform from the filter cake. Place the filter cake and the paper in a blending jar containing 250 milliliters of 0.1M phosphate buffer, pH 8.0, and blend for 10 minutes. Filter the blended material through a fast, porous, filter paper. Dilute the filtrate to obtain a solution for assay containing 1.0 microgram per milliliter. Its content of streptomycin is satisfactory if it contains not less than 85 percent of the number of milligrams per gram that it is represented to contain.

(ii) *Erythromycin content*. Proceed as directed in § 436.105 of this chapter, preparing the sample as follows: Place a representative quantity of the ointment (usually an entire container) in a blending jar and add sufficient methyl alcohol to give a volume of approximately 100 milliliters. Using a high-speed blender, blend the mixture for 2 to 3 minutes. Add 400 milliliters of 0.1M potassium phosphate buffer, pH 8.0, and blend for 2 to 3 minutes. Dilute the mixture to 1.0 microgram per milliliter (estimated) using 0.1M potassium phosphate buffer, pH 8.0. Its content of erythromycin is satisfactory if it contains not less than 85 percent of the number of milligrams per gram that it is represented to contain.

(2) *Moisture*. Proceed as directed in § 436.201 of this chapter.

[40 FR 13913, Mar. 23, 1975, as amended at 42 FR 21279, Apr. 26, 1977; 50 FR 19922, May 13, 1985]

§ 544.373 Streptomycin/dihydrostreptomycin ophthalmic and topical dosage forms.

§ 544.373a Streptomycin/dihydrostreptomycin ointment.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Streptomycin, ointment and dihydrostreptomycin

ointment are streptomycin or dihydrostreptomycin in a suitable and harmless ointment base, with or without suitable and harmless dispersing and suspending agents and preservatives. Their potency is not less than 5,000 µg per gram of ointment. The streptomycin used conforms to the requirements of § 444.70a(a)(1) (i), (vii), and (viii) of this chapter. The dihydrostreptomycin used conforms to the requirements of § 444.10a(a) of this chapter, except the standards for sterility, pyrogens, depressor substances, and loss on drying. Each other substance used, if its name is recognized in the U.S.P. or N.F., conforms to the standards prescribed therefor by such official compendium.

(2) *Packaging.* Streptomycin ointment and dihydrostreptomycin ointment shall be packaged in collapsible tubes which shall be well-closed containers as defined by the U.S.P., and each such tube shall not be larger than the 2-ounce size—but if the ointment is labeled solely for hospital use it may be packaged in immediate containers of glass that meet the test for tight containers as defined by the U.S.P. The composition of the immediate container and closure shall be such as will not cause any change in the strength, quality, or purity of the contents beyond any limit therefor in applicable standards; but minor changes that are normal and unavoidable in good packaging, storage, and distribution practice shall be disregarded.

(3) *Labeling.* In addition to the labeling requirements prescribed by § 510.55 of this chapter, each package shall bear on its outside wrapper or container and the immediate container the statement, "Expiration date _____", the blank being filled in with the date that is 24 months after the month during which the batch was certified.

(4) *Requests for certification; samples.* (i) In addition to complying with the requirements of § 514.50 of this chapter, a person who requests certification of a batch of streptomycin ointment or dihydrostreptomycin ointment shall submit with his request a statement showing the batch mark, the number of packages of each size in such batch, the batch mark and

(unless it was previously submitted) the date on which the latest assay of the streptomycin used in making such batch was completed, the quantity of each ingredient used in making the batch, the date on which the latest assay of the drug constituting such batch was completed, and that each component of the ointment base used conforms to the requirements prescribed therefor, if any, by this section.

(ii) Except as otherwise provided by paragraph (a)(4)(iv) of this section such person shall submit in connection with his request, results of the tests and assays. These tests and assays shall be made on an accurately representative sample and shall consist of the following:

(a) The batch; potency.

(b) The streptomycin or dihydrostreptomycin used in making the batch; potency, pH, streptomycin content if it is dihydrostreptomycin and crystallinity if it is crystalline dihydrostreptomycin sulfate.

(iii) Except as otherwise provided by paragraph (a)(4)(iv) of this section such person shall submit in connection with his request, in the quantities hereinafter indicated, accurately representative samples of the following:

(a) The batch; one immediate container for each 5,000 immediate containers in the batch, but in no case less than five immediate containers unless each such container is packaged for hospital use and contains more than 2 ounces, in which case the sample shall consist of approximately 1 ounce of ointment for each 5,000 immediate containers in the batch, but in no case less than five 1-ounce portions. Such sample shall be collected by taking single immediate containers or 1-ounce portions at such intervals throughout the entire time of packaging the batch that the quantities packaged during the intervals are approximately equal.

(b) The streptomycin or dihydrostreptomycin used in making the batch; five packages containing approximately equal portions of not less than 0.5 gram each.

(c) In case of an initial request for certification, the ingredients used in making the ointment base of the batch: one package of each containing

approximately 200 grams, except for the suspending and dispersing agents used, in which case the sample shall consist of approximately 5 grams.

(iv) No result referred to in paragraph (a)(4)(ii)(b) of this section, and no sample referred to in paragraph (a)(4)(iii)(b) of this section, is required if such result or sample has been previously submitted.

(b) *Tests and methods of assay*—(1) *Streptomycin content.* Proceed as directed in § 436.105 of this chapter, preparing the sample as follows: Accurately weigh the tube and contents and squeeze approximately 1.0 gram into a blending jar containing 50 milliliters of 0.1M potassium phosphate buffer (pH 7.8 to 8.0). Re-weigh the tube to obtain weight of ointment used in the test. Using a high-speed blender, blend the mixture for 3 minutes. Dilute an aliquot of the mixture to contain 100 micrograms of streptomycin base (estimated) per milliliter. Transfer 1.0 milliliter of this solution to a 100-milliliter flask and make up to volume with 0.1M potassium phosphate buffer (pH 7.8 to 8.0). Use this last dilution in the assay for potency. The potency of streptomycin ointment is satisfactory if it contains not less than 85 percent of the number of micrograms of streptomycin base per gram it is represented to contain.

(2) *Dihydrostreptomycin content.* Proceed as directed in paragraph (b)(1) of this section, using the dihydrostreptomycin working standard as a standard of comparison. Its content of dihydrostreptomycin is satisfactory if it contains not less than 85 percent of the number of micrograms of dihydrostreptomycin base per gram it is represented to contain.

(Secs. 507, 512(n), 701(f) and (g), 52 Stat. 1056-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371(f) and (g)))
[42 FR 21279, Apr. 26, 1977, as amended at 46 FR 60569, Dec. 11, 1981; 50 FR 19922, May 13, 1985]

§ 544.373b Streptomycin/dihydrostreptomycin-polymyxin-neomycin ointment.

(a) *Requirements for certification*—

(1) *Standards of identity, strength, quality, and purity.* Streptomycin-polymyxin-neomycin ointment and dihydrostreptomycin-polymyxin-neomycin ointment are streptomycin or dihydrostreptomycin, polymyxin, and neomycin in a suitable and harmless ointment base, with or without one or more suitable sulfonamides, and with or without suitable and harmless dispersing and suspending agents. Their moisture content is not more than 1 percent. Their potency is such that when used as directed in their labeling each dose shall contain not less than 250 milligrams of streptomycin or dihydrostreptomycin, 100,000 units of polymyxin B, and 150 milligrams of neomycin. The streptomycin used conforms to the requirements of § 444.70a(a)(1) (i), (vi), (vii), and (viii) of this chapter. The dihydrostreptomycin used conforms to the requirements of § 444.10a(a) of this chapter, except the standards for sterility, pyrogens, and depressor substances. The polymyxin B used conforms to the requirements prescribed for polymyxin B by § 448.30 of this chapter. The neomycin used conforms to the standards prescribed by § 444.42a(a)(1)(i), (v) and (vi) of this chapter. Each other substance used, if its name is recognized in the U.S.P. or N.F., conforms to the standards prescribed therefor by such official compendium.

(2) *Packaging.* Each batch of ointment shall be packaged in collapsible tubes which shall be well-closed containers as defined by the U.S.P. The composition of the immediate container shall be such as will not cause any change in the strength, quality, or purity of the contents beyond any limit therefor in applicable standards, except that minor changes so caused that are normal and unavoidable in good packaging, storage, and distribution practice shall be disregarded.

(3) *Labeling.* Each package shall bear on its label or labeling, as hereinafter indicated, the following:

(i) On the outside wrapper or container and the immediate container:

(a) The batch mark.

(b) The number of milligrams of streptomycin or dihydrostreptomycin, the number of milligrams of neomycin, and the number of units of polymyxin B in each gram of the batch.

(c) If the batch contains one or more sulfonamides, the name and quantity

of each such ingredient per gram of the batch.

(d) The statement "For veterinary use only".

(e) The statement "Expiration date _____", the blank being filled in with the date that is 18 months after the month during which the batch was certified: *Provided, however*, That such expiration date may be omitted from the immediate container if it contains a single dose and it is packaged in an individual wrapper or container.

(ii) On the circular or other labeling within or attached to the package, adequate directions and warnings for the veterinary use of such drug by the laity. Such circular or other labeling may also bear a statement that a brochure or other printed matter containing information for other veterinary uses of such drug by a veterinarian licensed by law to administer it will be sent to such veterinarian on request.

(4) *Requests for certification; samples.* (i) In addition to complying with the requirements of § 514.50 of this chapter, a person who requests certification of a batch shall submit with his request a statement showing the batch mark and (unless they were previously submitted) the dates on which the latest assays of the streptomycin or dihydrostreptomycin, polymyxin B, in neomycin used in making such batch were completed; the quantity of each such ingredient used in making the batch, the date on which the latest assay of the drug comprising such batch was completed, and a statement that each ingredient used in making the batch conforms to the requirements prescribed therefor by this section.

(ii) Except as otherwise provided by paragraph (a)(4)(iv) of this section, such person shall submit in connection with his request results of the tests and assays listed after each of the following made by him on an accurately representative sample of:

(a) The batch: Potency and moisture.

(b) The streptomycin or dihydrostreptomycin used in making the batch: Potency, pH, streptomycin content if it is dihydrostreptomycin, and

crystallinity if it is crystalline dihydrostreptomycin sulfate.

(c) The polymyxin B used in making the batch: Potency.

(d) The neomycin used in making the batch: Potency, moisture, and pH.

(iii) Except as otherwise provided by paragraph (a)(4)(iv) of this section, such person shall submit in connection with his request, in the quantities hereinafter indicated, accurately representative samples of the following:

(a) The batch: 1 immediate container for each 5,000 immediate containers in the batch, but in no case less than 7 immediate containers, collected by taking single immediate containers at such intervals throughout the entire time of packaging the batch that the quantities packaged during the intervals are approximately equal.

(b) The streptomycin or dihydrostreptomycin used in making the batch: six packages, each containing approximately equal portions of not less than 0.5 gram.

(c) The polymyxin B used in making the batch: 5 packages containing approximately equal portions of not less than 0.5 gram each.

(d) The neomycin used in making the batch: 5 packages containing approximately equal portions of not less than 0.5 gram each.

(e) In case of an initial request for certification, the ingredients used in making the batch: 1 package of each ointment-base ingredient, containing approximately 200 grams; 1 package of each suspending or dispersing agent used, containing approximately 5 grams; 1 package of each sulfonamide used, containing approximately 5 grams.

(iv) The results referred to in paragraph (a)(4)(ii)(b), (c), and (d) of this section and the samples referred to in paragraph (a)(4)(iii)(b), (c), and (d) of this section are not required if such results or samples have been previously submitted.

(b) *Tests and methods of assay—(1) Potency—(i) Streptomycin content.* Proceed as directed in § 436.105 of this chapter, preparing the sample in one of the following ways:

(a) *Extraction.* Place a convenient sized representative quantity of the sample in a separatory funnel contain-

ing approximately 50 milliliters of peroxide-free ether. Shake the sample and ether until homogeneous. Add a 20-milliliter portion of 0.1M potassium phosphate buffer, pH 8.0, and shake well. Remove the buffer layer and repeat the extraction with 20-milliliter portions of buffer at least three times and any additional times that may be necessary to insure complete extraction of the antibiotic. Combine the extractives and make the appropriate estimated dilutions in 0.1M potassium phosphate buffer, pH 8.0.

(b) *Blending.* Place a convenient sized representative quantity of the sample in a blending jar containing 1.0 milliliter of a 10-percent aqueous solution of polysorbate 80 and sufficient 0.1 M potassium phosphate buffer, pH 8.0, to give a volume of 200 milliliters. Using a high-speed blender, blend for 2 minutes and then make the appropriate estimated dilutions with buffer. Its content of streptomycin is satisfactory if it contains not less than 85 percent of the number of milligrams per gram that it is represented to contain.

(ii) *Dihydrostreptomycin content.* Proceed as directed in paragraph (b)(1) of this section, using the dihydrostreptomycin working standard as a standard of comparison. Its content of dihydrostreptomycin is satisfactory if it contains not less than 85 percent of the number of milligrams per gram that it is represented to contain.

(iii) *Polymyxin content.* Proceed as directed in § 436.105 of this chapter, preparing the sample as follows:

(a) Place a convenient-sized representative quantity of the sample in a separatory funnel containing approximately 50 milliliters of peroxide-free ether. Shake the sample and ether until homogeneous. Add 25 milliliters of 10-percent potassium phosphate buffer, pH 6.0, containing 2 grams of K_2HPO_4 and 8 grams of KH_2PO_4 , in each 100 milliliters, and shake. Remove the buffer layer and repeat the extraction with 25-milliliter portions of buffer at least three times and any additional times that may be necessary to insure complete extraction of the antibiotic. Combine the extractives and make the proper estimated dilutions in 10-percent potassium phosphate buffer pH 6.0, to give a con-

centration of 10 units per milliliter (estimated). If the sample contains a water-soluble base, accurately weigh a representative sample and place in a blending jar containing 1 milliliter of polysorbate 80 and sufficient 10-percent potassium phosphate buffer, pH 6.0, to give a final volume of 200 milliliters. Use a high-speed blender and blend the mixture for 2 minutes. Make the proper estimated dilutions, using 10-percent potassium phosphate buffer, pH 6.0.

(b) The standard curve is prepared in the following concentrations: 6.4, 8.0, 10.0, 12.5, and 15.6 units per milliliter in 10 percent potassium phosphate buffer, pH 6.0. The 10 units per milliliter concentration is used as the reference point. Calculate from the quantity of neomycin that would be present when the sample is diluted to contain 10 units of polymyxin (labeled potency) per milliliter. Prepare the polymyxin standard curve by adding the calculated quantity of neomycin to each concentration of polymyxin used for the curve. Use the standard curve to calculate the polymyxin content. Its content of polymyxin is satisfactory if it contains not less than 85 percent of the number of units that it is represented to contain.

(iv) *Neomycin content.* Proceed as directed in § 436.105 of this chapter:

(a) Prepare the sample as directed in paragraph (b)(1)(i)(a) of this section or by a blending technique as follows: Place a convenient sized representative quantity of the sample in a blending jar containing 1.0 milliliter of a 0.3-percent aqueous solution of dioctyl sodium sulfosuccinate and sufficient 0.1 M potassium phosphate buffer, pH 8.0, to give a volume of 200 milliliters. Using a high-speed blender, blend for 5 minutes and then make the appropriate estimated dilutions with buffer.

(b) Use as the test organism the Food and Drug Administration dihydrostreptomycin-(and streptomycin-) resistant strain of *Staphylococcus aureus* (American Type Culture Collection 6538-PR)¹ which is grown and

¹ Available from: American Type Culture Collection, 12301 Parklawn Dr., Rockville, Md. 20852.

maintained on media containing 1,000 micrograms of dihydrostreptomycin per milliliter of agar. Its content of neomycin is satisfactory if it contains not less than 85 percent of the number of milligrams per gram that it is represented to contain.

(2) *Moisture*. Proceed as directed in § 436.201 of this chapter.

(Secs. 507, 512(n), 701(f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371(f) and (g)))

[40 FR 13913, Mar. 27, 1975, as amended at 42 FR 21280, Apr. 26, 1977; 46 FR 60569, Dec. 11, 1981; 50 FR 19922, May 13, 1985; 50 FR 26197, June 25, 1985]

Subparts D—H [Reserved]

Subpart I—Certain Other Dosage Forms

§ 544.973b Streptomycin/dihydrostreptomycin solution for inhalation therapy.

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality, and purity*. Streptomycin solution for inhalation therapy and dihydrostreptomycin solution for inhalation therapy is a suitable and harmless aqueous-organic solution of streptomycin or dihydrostreptomycin, with or without suitable and harmless preservatives, colorings, volatile oils, flavorings, buffer substances, and stabilizing agents. Its potency is not less than 50 milligrams per milliliter. Its pH is not less than 5.0 and not more than 8.0. The streptomycin or dihydrostreptomycin used conforms to the standards prescribed by § 444.10a(a)(1) of this chapter or § 444.70a(a)(1) of this chapter, except the standards for sterility, pyrogens, and depressor substances, or to the standards prescribed by § 539.170(a)(1). Each other substance used, if its name is recognized in the U.S.P. or N.F., conforms to the standards prescribed therefor by such official compendium.

(2) *Packaging*. In all cases the immediate container shall be a tight container as defined by the U.S.P. The composition of the immediate container shall be such as will not cause any change in the strength, quality, or purity of the contents beyond any limit therefore in applicable stand-

ards, except that minor changes so caused that are normal and unavoidable in good packaging, storage, and distribution practice shall be disregarded.

(3) *Labeling*. Each package shall bear on its label or labeling, as hereinafter indicated, the following:

(i) On the outside wrapper or container and the immediate container:

(a) The batch mark.

(b) The number of milligrams of streptomycin or dihydrostreptomycin in each milliliter of the batch.

(c) The statement "Expiration date —", the blank being filled in with the date that is 12 months after the month during which the batch was certified.

(d) The name and quantity of each preservative used.

(e) The statement "For veterinary use only".

(f) The statement "Warning—Not for use in animals which are raised for food production".

(4) *Requests for certification; samples*. (i) In addition to complying with the requirements of § 514.50 of this chapter, a person who requests certification of a batch shall submit with his request a statement showing the batch mark, the number of packages of each size in the batch and the number of milligrams of streptomycin or dihydrostreptomycin per milliliter in the batch. Such request shall be accompanied or followed by the results of tests and assays made by him on the batch for potency and pH.

(ii) Such person shall also submit with his request, in the quantities hereinafter indicated, accurately representative samples of the following:

(a) The batch: 1 immediate container for each 5,000 immediate containers in the batch, but in no case less than 5 immediate containers.

(b) In case of an initial request for certification, each other ingredient used in making the batch: 1 package of each containing approximately 5 grams.

(b) *Tests and methods of assay—(1) Potency*. Proceed as directed in § 444.70a(b)(1) of this chapter, except that if it contains dihydrostreptomycin use the dihydrostreptomycin working standard as the standard of com-

parison. Its potency is satisfactory if it contains not less than 90 percent of the number of milligrams per milliliter that it is represented to contain.

(2) *pH*. Proceed as directed in § 436.202 of this chapter, using the undiluted drug.

(Secs. 507, 512(n), 701(f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371(f) and (g)))

[40 FR 13913, Mar. 27, 1975, as amended at 42 FR 21281, Apr. 26, 1977; 46 FR 60569, Dec. 11, 1981]

PART 546—TETRACYCLINE ANTIBIOTIC DRUGS FOR ANIMAL USE

Subpart A—Oral Dosage Forms

Sec.
546.110 Chlortetracycline oral dosage forms.

546.110a Crude chlortetracycline.

546.110b Chlortetracycline seed.

546.110c Chlortetracycline powder (chlortetracycline hydrochloride powder).

546.110d Chlortetracycline tablets and boluses.

546.110e—546.110f [Reserved]

546.110g Chlortetracycline hydrochloride in oil oral.

546.113 Chlortetracycline bisulfate oral dosage forms.

546.113a Chlortetracycline bisulfate soluble powder.

546.113b Chlortetracycline bisulfate-sulfamethazine bisulfate soluble powder.

546.180 Tetracycline oral dosage forms.

546.180a Tetracycline hydrochloride capsules.

546.180b Tetracycline tablets.

546.180c Tetracycline boluses.

546.180d Tetracycline soluble powder.

546.180e Tetracycline oral liquid.

546.180f Tetracycline oral suspension.

546.180g Tetracycline phosphate complex and sodium novobiocin capsules.

546.180h Tetracycline hydrochloride and sodium novobiocin tablets.

546.180i Tetracycline hydrochloride, sodium novobiocin, and prednisolone tablets.

Subpart B—[Reserved]

Subpart C—Ophthalmic and Topical Dosage Forms

546.312 Chlortetracycline/tetracycline ophthalmic and topical dosage forms.

Sec.

546.312a Chlortetracycline-neomycin-streptomycin/dihydrostreptomycin ointment; tetracycline hydrochloride-neomycin-streptomycin/dihydrostreptomycin ointment.

546.312b Chlortetracycline/chlortetracycline hydrochloride/tetracycline hydrochloride ophthalmic.

546.381 Tetracycline hydrochloride ophthalmic and topical dosage forms.

546.381a Tetracycline hydrochloride-neomycin topical spray ointment.

546.381b Tetracycline hydrochloride-neomycin in oil suspension.

Subparts D—F [Reserved]

Subpart G—Rectal Dosage Forms

546.713 Chlortetracycline/chlortetracycline hydrochloride/tetracycline hydrochloride suppositories.

AUTHORITY: Sec. 512, 82 Stat. 343-351 (21 U.S.C. 360b); 21 CFR 5.10, 5.83.

SOURCE: 40 FR 13924, Mar. 27, 1975, unless otherwise noted.

Subpart A—Oral Dosage Forms

§ 546.110 Chlortetracycline oral dosage forms.

§ 546.110a Crude chlortetracycline.

(a) *Requirements for certification—*
(1) *Standards of identity, strength, quality, and purity.* Crude chlortetracycline oral is crude chlortetracycline with suitable and harmless diluents, with or without buffer substances and suspending and dispersing agents (and with or without one or more essential vitamins and mineral substances for nutritive purposes). It contains not less than 2 grams of chlortetracycline activity per pound, except it shall contain 100 grams of chlortetracycline activity per pound if it is intended for use in the treatment of psittacosis in psittacine birds (parrots, macaws, and cockatoos). Its moisture content is not more than 6 percent.

(2) *Packaging.* In all cases the immediate container shall be a well-closed container as defined by the U.S.P. and shall be of such composition as will not cause any change in the strength, quality, or purity of the contents beyond any limit therefor in applicable standards, except that minor changes so caused that are normal and

unavoidable in good packaging, storage, and distribution practice shall be disregarded. Each such container shall contain not more than 100 pounds.

(3) *Labeling.* Each package shall bear on its label or labeling, as herein-after indicated, the following:

(i) On the outside wrapper or container and the immediate container:

(a) The batch mark.

(b) The number of grams of chlortetracycline in each pound of the batch.

(c) The statement "For oral veterinary use only" and if it is intended for use in the treatment of psittacosis in psittacine birds, a statement to the effect that wet mash prepared with the drug should be discarded after 24 hours.

(d) The statement "Expiration date—", the blank being filled in with the date which is 24 months after the month during which the batch was certified.

(ii) On the circular or other labeling within or attached to the package:

(a) Adequate directions and warnings for the veterinary use of such drug by the laity.

(b) If it is intended for use in animals raised for food production, labeling in accordance with the requirements of regulations in Part 558 of this chapter.

(4) *Request for certification; samples.* (i) In addition to complying with § 514.50 of this chapter, a person who requests certification of a batch shall submit with his request a statement showing the batch mark, the number of packages of each size in such batch, the number of grams of chlortetracycline in each pound of the batch, and the quantity of each other ingredient used in making the batch, and the date on which the latest assay of the batch was completed. Such request shall be accompanied or followed by the results of tests and assays made by him on the batch for average potency and average moisture.

(ii) Such person shall submit in connection with his request a sample of the batch consisting of 1 ounce for each 3,000 pounds in the batch, but in no case less than five 1-ounce portions, collected by taking single 1-ounce portions at such intervals throughout the entire time of packaging the batch

that the quantities packaged during the intervals are approximately equal.

(b) *Tests and methods of assay—(1) Potency.* Accurately weigh approximately 3.0 grams of the sample and place in a blending jar containing 200 milliliters of an acid-acetone solution prepared with 1 part 4 N HCl, 6 parts distilled water, and 13 parts acetone. Blend for 3 minutes. Using an aliquot of the liquid, make the proper estimated dilutions in sterile distilled water, shake well, and proceed as directed in § 436.106 of this chapter. Its content of chlortetracycline is satisfactory if it contains not less than 85 percent of the number of grams that it is represented to contain.

(2) *Moisture.* Proceed as directed in § 436.200(b) of this chapter.

(Secs. 507, 512, 59 Stat. 463 as amended; sec. 572, 82 Stat. 343-351 (21 U.S.C. 357, 360b))

[40 FR 13924, Mar. 27, 1975, as amended at 41 FR 11011, Mar. 15, 1976; 43 FR 11177, Mar. 17, 1978]

§ 546.110b Chlortetracycline seed.

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality, and purity.* Chlortetracycline seed is dehulled millet seed containing chlortetracycline. It contains 0.5 milligram of chlortetracycline per gram. Its moisture content is not more than 10 percent. The chlortetracycline used conforms to the requirements prescribed therefor by § 446.10(a)(1) of this chapter, or to the requirements prescribed by § 546.110c(a)(1). Each other substance used, if its name is recognized in the U.S.P. or N.F., conforms to the standards prescribed therefor by such official compendium.

(2) *Packaging.* In all cases the immediate container shall be a well-closed container as defined by the U.S.P. and shall be of such composition as will not cause any change in the strength, quality, or purity of the contents beyond any limit therefor in applicable standards, except that minor changes so caused that are normal and unavoidable in good packaging, storage, and distribution practice shall be disregarded.

(3) *Labeling.* Each package shall bear on its label or labeling, as herein-after indicated, the following:

(i) On the outside wrapper or container and the immediate container:

(a) The batch mark.
(b) The number of milligrams of chlortetracycline in each gram of the batch.

(c) The statement "For oral veterinary use only".

(d) The statement "Expiration date _____", the blank being filled in with the date that is 12 months after the month during which the batch was certified, except that the blank may be filled in with the date that is 24 months after the month during which the batch was certified if the person who requests certification has submitted to the Commissioner results of tests and assays showing that after having been stored for such period of time such drug as prepared by him complies with the standards prescribed by paragraph (a)(1) of this section.

(ii) On the circular or other labeling within or attached to the package, adequate directions and warnings for the use of such drug by the laity. Such circular or other labeling may also bear a statement that a brochure or other printed matter containing information for other veterinary uses of such drug by a veterinarian licensed by law to administer it will be sent to such veterinarian on request.

(4) *Request for certification; samples.* (i) In addition to complying with the requirements of § 514.50 of this chapter, a person who requests certification of a batch shall submit with his request a statement showing the batch mark, the number of packages of each size in such batch, the batch mark and (unless it was previously submitted) the date on which the latest assay of the chlortetracycline used in making such batch was completed, the number of milligrams in each immediate container, the quantity of each ingredient used in making the batch, the date on which the latest assay of the drug comprising such batch was completed, and a statement that each ingredient used in making the batch conforms to the requirements prescribed therefor, if any, by this section.

(ii) Except as otherwise provided in paragraph (a)(4)(iv) of this section, such person shall submit in connection

with his request results of the tests and assays listed after each of the following, made by him on an accurately representative sample of:

(a) The batch: Potency and moisture.

(b) The chlortetracycline used in making the batch: Potency, moisture, pH, and crystallinity.

(iii) Except as otherwise provided by paragraph (a)(4)(iv) of this section, such person shall submit in connection with his request, in the quantities hereinafter indicated, accurately representative samples of the following:

(a) The batch: One container for each 5,000 containers in the batch, but in no case less than five immediate containers. Such sample shall be collected by taking single immediate containers at such intervals throughout the entire time the containers are being filled that the quantities filled during the intervals are approximately equal.

(b) The chlortetracycline used in making the batch: 10 packages, each containing approximately equal portions of not less than 60 milligrams, packaged in accordance with the requirements of § 446.10a(a)(2) of this chapter.

(c) In case of an initial request for certification, each other ingredient used in making the batch: One package of each, containing approximately 5 grams.

(iv) The results referred to in paragraph (a)(4)(ii)(b) of this section and the sample referred to in paragraph (a)(4)(iii)(b) of this section are not required if such results or sample has been previously submitted.

(b) *Tests and methods of assay—(1) Potency.* Accurately weigh approximately 10 grams of the sample and place in a blending jar containing 500 milliliters of 0.01 N HCl. Blend for 3 minutes. Using an aliquot of the liquid, make the proper estimated dilutions in sterile distilled water, shake well, and proceed as directed in § 436.106 of this chapter. Its content of chlortetracycline is satisfactory if it contains not less than 85 percent of the number of milligrams per gram that it is represented to contain.

(2) *Moisture.* Proceed as directed in § 436.200b of this chapter.

§ 546.110c

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(Secs 507, 512, 59 Stat. 463 as amended; sec. 572, 82 Stat. 343-351 (21 U.S.C. 357, 360b))
[40 FR 13924, Mar. 27, 1975, as amended at 41 FR 10886, Mar. 15, 1976; 43 FR 11178, Mar. 17, 1978; 50 FR 19922, May 13, 1985]

§ 546.110c Chlortetracycline powder
(chlortetracycline hydrochloride powder).

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality, and purity.* Chlortetracycline powder, (chlortetracycline hydrochloride powder), tetracycline hydrochloride powder, and tetracycline powder, and tetracycline powder are crystalline chlortetracycline hydrochloride, tetracycline hydrochloride, or tetracycline, with or without glucosamine hydrochloride and with or without suitable and harmless buffer substances, preservatives, diluents, colorings, and flavorings. It may contain one or more suitable and harmless vitamin substances. The content of chlortetracycline or tetracycline hydrochloride or tetracycline is not less than 15 milligrams per gram of powder. The moisture content of chlortetracycline powder or tetracycline hydrochloride powder is not more than 2 percent. The moisture content of tetracycline powder is not more than 7.5 percent. The chlortetracycline used conforms to the requirements of § 446.10(a)(1) of this chapter. The tetracycline hydrochloride used conforms to the requirements of § 446.81(a)(1) of this chapter. The tetracycline used conforms to the requirements of § 446.80(a)(1) of this chapter. Each other substance used, if its name is recognized in the U.S.P. or N.F., conforms to the standards prescribed therefor by such official compendium.

(2) *Packaging.* It is packaged for dispensing and intended solely for veterinary use: In all cases the immediate container shall be a tight container as defined by the U.S.P. The composition of the immediate container shall be such as will not cause any change in the strength, quality, or purity of the contents beyond any limits therefor in applicable standards, except that minor changes so caused which are normal and unavoidable in good packaging, storage, and distribution practice shall be disregarded. Its label and

labeling shall comply with all the requirements prescribed by paragraph (a)(3) of this section, except that in lieu of the statement "Caution: Federal law prohibits dispensing without prescription", each package shall include information containing directions and warnings adequate for the veterinary use of the drugs by the laity.

(3) *Labeling.* In addition to the labeling requirements prescribed by § 201.105 of this chapter (regulations issued under section 502(f) of the act), each package shall bear on the outside wrapper or container and the immediate container, as hereinafter indicated, the following:

(i) The statement "Expiration date—", the blank being filled in with the date that is 60 months after the month during which the batch was certified it is chlortetracycline hydrochloride powder; or if it is tetracycline hydrochloride powder or tetracycline powder the blank is filled in with the date that is 24 months after the month during which the batch was certified, except that the blank may be filled in with the date that is 36 months, 48 month, or 60 months after the month during which the batch was certified if the person who requests certification has submitted to the Commissioner results of tests and assays showing that after having been stored for such period of time such drug as prepared by him complies with the standards prescribed by paragraph (a)(1) of this section.

(ii) If it contains, in addition to chlortetracycline hydrochloride, tetracycline hydrochloride, or tetracycline, one or more of the other active ingredients specified in paragraph (a)(1) of this section after the name "chlortetracycline powder", "tetracycline hydrochloride powder", or "tetracycline powder", wherever such name appears the words "with—" (the blank being filled in with the established name of each other such ingredient)", in juxtaposition with such name. If it is intended for use in animals raised for food production, it shall also be labeled in accordance with the requirements of paragraph (c) of this section.

(4) *Request for certification; samples.* (i) In addition to complying with

the requirements of § 514.50 of this chapter, a person who requests certification of a batch shall submit with his request a statement showing the batch mark, the number of packages of each size in such batch, the batch mark and (unless it was previously submitted) the date on which the latest assay of the chlortetracycline, tetracycline hydrochloride or tetracycline used in making such batch was completed, the number of milligrams in each immediate container, the quantity of each ingredient used in making the batch, the date on which the latest assay of the drug constituting such batch was completed, and a statement that each ingredient used in making the batch conforms to the requirements prescribed therefor, if any, by this section.

(ii) Except as otherwise provided in paragraph (a)(4)(iv) of this section, such person shall submit in connection with his request, results of the tests and assays listed after each of the following, made by him on an accurately representative sample of:

(a) The batch; potency and moisture.

(b) The chlortetracycline, tetracycline hydrochloride, or tetracycline used in making the batch: potency, moisture, pH, and crystallinity, and absorptivity if it is tetracycline hydrochloride or tetracycline.

(iii) Except as otherwise provided by paragraph (a)(4)(iv) of this section, such person shall submit in connection with his request, in the quantities hereinafter indicated, accurately representative samples of the following:

(a) The batch: one immediate container for each 5,000 containers in the batch, but in no case less than 5 immediate containers, unless each such container is packaged to contain more than 10 grams, in which case the sample shall consist of 1.0 gram for each 5,000 immediate containers in the batch, but in no case less than five 1.0-gram portions; except if it is intended for use as an ingredient in the drinking water of animals each portion in the sample submitted shall consist of 1 ounce in lieu of 1.0 gram. Such sample shall be collected by taking single immediate containers, 1.0-gram portions, or 1-ounce portions at such intervals

throughout the entire time the containers are being filled so that the quantities filled during the intervals are approximately equal.

(b) The chlortetracycline, tetracycline hydrochloride, or tetracycline used in making the batch: 10 packages, each containing approximately equal portions of not less than 60 milligrams, packaged in accordance with the requirements of § 510.55 of this chapter.

(c) In case of an initial request for certification, each other ingredient used in making the batch: one package of each containing approximately 5 grams.

(iv) No result referred to in paragraph (a)(4)(ii)(b) of this section, and no sample referred to in paragraph (a)(4)(iii)(b) of this section, is required if such result or sample has been previously submitted.

(b) *Tests and methods of assay*—(1) *Potency*. Using a 3.0-gram sample or the entire contents of the immediate container for each determination, proceed as directed in § 446.10(b)(1) of this chapter if it is chlortetracycline powder. If it is tetracycline powder, blend a 3.0-gram sample as directed in § 446.181d(b)(1) of this chapter, or reconstitute in the immediate container as directed in the labeling of the drug. Transfer an appropriate aliquot of 1.0 milliliter to 5.0 milliliters to a 100-milliliter volumetric flask and make to mark with 0.1N HCl. Withdraw an aliquot from the volumetric flask and dilute to 0.24 microgram per milliliter, using sterile distilled water and proceed as directed in § 446.81(b)(1) of this chapter. The average potency of the powder is satisfactory if it contains not less than 85 percent of the number of milligrams of chlortetracycline or tetracycline hydrochloride or tetracycline per gram or per immediate container that it is represented to contain.

(2) *Moisture*. Proceed as directed in § 436.200(b) of this chapter.

(c) *Conditions of marketing*—(1) *Specifications*. Meets the requirements of paragraph (a) of this section.

(2) *Sponsor*. No. 000010 in § 510.600(c) of this chapter for conditions of use as in paragraphs (c)(5) (iii) and (iv) of this section; No. 010042 in

§ 510.600(c) of this chapter for conditions of use as in paragraphs (c)(5) (i) and (ii) of this section; No. 054273 in § 510.600(c) of this chapter for conditions of use as in paragraph (c)(5)(v) of this section.

(3) *Special considerations.* The quantities of antibiotic in paragraph (c)(5) of this section refer to the activity of the master standard.

(4) *Related tolerances.* See § 556.150 of this chapter.

(5) *Conditions of use.* (i) It is used in drinking water as follows:

(a) *Chickens.* Used as chlortetracycline hydrochloride or chlortetracycline bisulfate as follows:

(1) *Amount per gallon.* 100 milligrams.

(i) *Indications for use.* Prevention of chronic respiratory disease (air-sac infection), blue comb (nonspecific infectious enteritis).

(ii) *Limitations.* Not to be used for more than 14 consecutive days; as sole source of chlortetracycline.

(2) *Amount per gallon.* 200 milligrams.

(i) *Indications for use.* Treatment of chronic respiratory disease (air-sac infection), blue comb (nonspecific infectious enteritis); prevention of synovitis.

(ii) *Limitations.* Not to be used for more than 14 consecutive days; as sole source of chlortetracycline.

(b) *Growing chickens.* Used as chlortetracycline hydrochloride or chlortetracycline bisulfate as follows:

(1) *Amount per gallon.* 1,000 milligrams.

(2) *Indications for use.* Aid in the control of mortality due to fowl cholera.

(3) *Limitations.* Not for laying chickens; not to be used for more than 14 consecutive days; withdraw 24 hours prior to slaughter; as sole source of chlortetracycline.

(c) *Chickens and turkeys.* Used as chlortetracycline hydrochloride or chlortetracycline bisulfate as follows:

(1) *Amount per gallon.* 400 milligrams.

(2) *Indications for use.* Control of synovitis.

(3) *Limitations.* Not for laying chickens; not to be used for more than

14 consecutive days; as sole source of chlortetracycline.

(d) *Turkeys.* Used as chlortetracycline hydrochloride or chlortetracycline bisulfate as follows:

(1) *Amount per gallon.* 100 milligrams.

(i) *Indications for use.* Prevention of blue comb (nonspecific infectious enteritis, mud fever), infectious sinusitis, hexamitiasis.

(ii) *Limitations.* Not to be used for more than 14 consecutive days; as sole source of chlortetracycline.

(2) *Amount per gallon.* 200 milligrams.

(i) *Indications for use.* Treatment of blue comb (nonspecific infectious enteritis, mud fever), infectious sinusitis, hexamitiasis; prevention of synovitis.

(ii) *Limitations.* Not to be used for more than 14 consecutive days; as sole source of chlortetracycline.

(e) *Swine.* Used as chlortetracycline hydrochloride as follows:

(1) *Amount per gallon.* 100 to 200 milligrams.

(i) *Indications for use.* As an aid in prevention of bacterial enteritis.

(ii) *Limitations.* Administer for not more than 46 days; do not slaughter animals for food within 24 hours of treatment; prepare a fresh solution daily; as sole source of chlortetracycline.

(2) *Amount per gallon.* 200 to 400 milligrams.

(i) *Indications for use.* As an aid in prevention of bacterial pneumonia; for treatment of bacterial enteritis.

(ii) *Limitations.* Administer for not more than 46 days; do not slaughter animals for food within 24 hours of treatment; prepare a fresh solution daily; as sole source of chlortetracycline.

(3) *Amount per gallon.* 400 to 600 milligrams.

(i) *Indications for use.* For treatment of bacterial pneumonia.

(ii) *Limitations.* Administer for not more than 24 days; do not slaughter animals for food within 24 hours of treatment; prepare a fresh solution daily; as sole source of chlortetracycline.

(ii) It is used as chlortetracycline hydrochloride as a drench for calves as follows:

(a) *Amount.* Two milligrams per pound of body weight.

(b) *Indications for use.* For treatment of bacterial pneumonia, bacterial diarrhea, and shipping fever.

(c) *Limitations.* Administer 2 milligrams per pound of body weight per day for not more than 5 days; do not slaughter animals for food within 3 days of treatment; prepare a fresh solution daily; as sole source of chlortetracycline.

(iii) *Swine:* It is used as chlortetracycline hydrochloride in drinking water as follows:

(a) *Amount.* One gram per gallon to provide approximately 10 milligrams per pound of body weight daily.

(b) *Indications for use.* It is used as an aid in the control and treatment of bacterial enteritis (scours) caused by *Escherichia coli* and bacterial pneumonia associated with *Pasteurella* spp., *Hemophilus* spp., and *Klebsiella* spp.

(c) *Limitations.* Prepare a fresh solution twice daily, as sole source of chlortetracycline, administer for not more than 45 days, do not slaughter animals for food within 5 days of treatment.

(iv) *Calves:* It is used as a chlortetracycline hydrochloride drench as follows:

(a) *Amount.* One level tablespoonful per each 98 pounds of body weight every 12 hours to provide approximately 10 milligrams per pound of body weight daily.

(b) *Indications for use.* It is used as an aid in the control and treatment of bacterial enteritis (scours) caused by *Escherichia coli* and bacterial pneumonia (shipping fever) associated with *Pasteurella* spp., *Hemophilus* spp., and *Klebsiella* spp.

(c) *Limitations.* As sole source of chlortetracycline, administer for not more than 5 days, do not slaughter animals for food within 24 hours of treatment.

(v) The following uses of chlortetracycline hydrochloride in drinking water are NAS/NRC reviewed and are deemed effective; applications for these uses need not include the effectiveness data specified by § 514.111 of this chapter:

(a) *Chickens—(1) Amount per gallon.* 200 to 400 milligrams.

(i) *Indications for use.* For the control of infectious synovitis caused by *M. synoviae*.

(ii) *Limitations.* Prepare fresh solution daily, as sole source of chlortetracycline, do not use for more than 14 days, do not slaughter animals for food within 24 hours of treatment, do not use in laying chickens.

(2) *Amount per gallon.* 400 to 800 milligrams.

(i) *Indications for use.* For the control of chronic respiratory disease (CRD) and air sac infections caused by *M. gallisepticum* and *E. coli*.

(ii) *Limitations.* Prepare fresh solution daily, as sole source of chlortetracycline, do not use for more than 14 days, do not slaughter animals for food within 24 hours of treatment, do not use in laying chickens.

(b) *Turkeys—(1) Amount per gallon.* 400 milligrams.

(i) *Indications for use.* For the control of infectious synovitis caused by *M. synoviae*.

(ii) *Limitation.* Prepared fresh solution daily, as sole source of chlortetracycline, do not use for more than 14 days, do not slaughter animals for food within 24 hours of treatment, for growing turkeys only.

(2) *Amount.* 25 milligrams per pound of body weight daily.

(i) *Indications for use.* For the control of complicating bacterial organisms associated with bluecomb (transmissible enteritis, coronaviral enteritis).

(ii) *Limitations.* Prepare fresh solution daily, as sole source of chlortetracycline, do not use for more than 14 days, do not slaughter animals for food within 24 hours of treatment, for growing turkeys only.

(c) *Swine—(1) Amount.* 10 milligrams per pound body weight daily in divided doses.

(2) *Indications for use.* For the control and treatment of bacterial enteritis (scours) caused by *E. coli* and *Salmonella* spp. and bacterial pneumonia associated with *Pasteurella* spp., *Hemophilus* spp., and *Klebsiella* spp.

(3) *Limitations.* Prepare fresh solution daily, as sole source of chlortetracycline, do not use more than 5 days,

do not slaughter animals for food within 5 days of treatment.

(d) *Calves, beef cattle, and nonlactating dairy cattle*—(1) *Amount.* 10 milligrams per pound daily in divided doses.

(2) *Indications for use.* For the control and treatment of bacterial enteritis (scours) caused by *E. coli* and *Salmonella* spp. and bacterial pneumonia (shipping fever complex) associated with *Pasteurella* spp., *Hemophilus* spp., and *Klebsiella* spp.

(3) *Limitations.* Prepare fresh solution daily, use as a drench, as sole source of chlortetracycline, do not use more than 5 days, do not slaughter animals for food within 24 hours of treatment, do not use in lactating cattle.

(Secs 507, 512, 59 Stat. 463 as amended; sec. 572, 82 Stat. 343-351 (21 U.S.C. 357, 360b))

[40 FR 13924, Mar. 27, 1975, as amended at 41 FR 23948, June 14, 1976; 43 FR 11178, Mar. 17, 1978; 49 FR 45423, Nov. 16, 1984; 50 FR 19922, May 13, 1985; 51 FR 28547, Aug. 8, 1986]

§ 546.110d Chlortetracycline tablets and boluses.

(a) *Requirements for certification*—

(1) *Standards of identity, strength, quality, and purity.* Chlortetracycline hydrochloride tablets and boluses, tetracycline hydrochloride tablets, and tetracycline tablets are tablets and boluses composed of crystalline chlortetracycline hydrochloride, tetracycline, or tetracycline phosphate complex, with or without one or more suitable and harmless buffer substances, preservatives, diluents, binders, lubricants, colorings, and flavorings. The potency of the drug is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams it is represented to contain. The moisture content of the tablets is not more than 3 percent, unless the person who requests certification has submitted to the Commissioner information adequate to prove that the drug is stable when it has a moisture content not exceeding 6 percent. The moisture content of the boluses is not more than 6 percent.

(2) *Exemption of chlortetracycline hydrochloride tablets from certifica-*

tion: Chlortetracycline hydrochloride tablets that conform to the requirements of § 446.110a(a)(1) of this chapter (except that it may contain one or more essential vitamin and mineral substances for nutritive purposes; and the chlortetracycline hydrochloride used in making the tablets may conform to § 546.110a(a)(1)) shall be exempt from the certification requirements of section 512(n) of the act, if they comply with all the following conditions:

(i) If the drug contains added vitamins or minerals, its label bears the name and quantity of each such substance and a statement that such substances are present only for furnishing additional vitamins and minerals while the birds are eating less feed.

(ii) The labels bear an expiration date that is not more than 24 months after the month during which the batch was last assayed and released by the manufacturer.

(iii) The label bears a statement that solutions prepared with the drug are stable for not more than 24 hours.

(iv) The circular or other labeling within or attached to the package bears information that only the antibiotic is intended for use in the prevention or treatment of the following conditions of parakeets and canaries, due to organisms sensitive to chlortetracycline, and further, bears directions and warnings adequate for such uses:

(a) Respiratory disease, bacterial (pneumonia, bronchitis, rhinitis).

(b) Infectious arthritis due to a filterable agent.

(c) Bacterial enteritis.

(d) Stimulate food intake, growth, and to maintain body weight.

(e) When intended for use in the conditions set forth in paragraph (a)(2)(iv) (a), (b), and (c) of this section, the potency must be such, that when used as directed in the labeling, each ounce of drinking water contains not less than 25 milligrams of chlortetracycline.

(f) When intended for use in the conditions set forth in paragraph (a)(2)(iv)(d) of this section, the potency must be such, that when used as directed in the labeling, each ounce of drinking water contains not less than 5.0 milligrams of chlortetracycline.

(3) Packaging. Unless each tablet is enclosed in a foil or plastic film and such enclosure is a tight container as defined by the U.S.P., except the provision that it shall be capable of tight reclosure, the immediate container shall be a tight container as so defined. The immediate container may also contain a desiccant separated from the tablets by a plug of cotton or other like material. The composition of the immediate container, or of the foil or film inclosure, shall be such as will not cause any change in the strength, quality, or purity of the contents beyond any limit therefor in applicable standards, except that minor changes so caused which are normal and unavoidable in good packaging, storage, and distribution practice shall be disregarded.

(4) Labeling. In addition to the labeling requirements prescribed by § 201.105 of this chapter (regulations issued under section 502(f) of the act), each package shall bear on the outside wrapper or container and the immediate container, as hereinafter indicated, the following: The statement "Expiration date ———", the blank being filled in with one of the following dates after the month during which the batch was certified:

(i) If chlortetracycline hydrochloride is used, 60 months.

(ii) If tetracycline hydrochloride is used, 48 months, except that the date that is 60 months may be used if the person who requests certification has submitted to the Commissioner results of tests and assays showing that after having been stored for such period of time such drug as prepared by him complies with the standards prescribed therefor by paragraph (a)(1) of this section.

(iii) If tetracycline is used, 36 months.

(iv) If tetracycline phosphate complex is used, 24 months, except that the blank may be filled in with the date that is 36 months, 48 months, or 60 months, after the month in which the batch was certified, if the person who requests certification has submitted to the Commissioner results of tests and assays showing that after having been stored for such period of time such drug as prepared by him

complies with the standards prescribed by paragraph (a)(1) of this section.

(5) Requests for certification; samples. (i) In addition to complying with the requirements of § 514.50 of this chapter, a person who requests certification of a batch shall submit with his request a statement showing the batch mark, the number of packages of each size in such batch, the batch mark and (unless it was previously submitted) the date on which the latest assay of the chlortetracycline, tetracycline hydrochloride, tetracycline or tetracycline phosphate complex used in making such batch was completed, the number of milligrams in each capsule, the quantity of each ingredient used in making the batch, the date on which the latest assay of the drug constituting such batch was completed, and a statement that each ingredient used in making the batch conforms to the requirements prescribed therefor, if any, by this section.

(ii) Except as otherwise provided in paragraph (a)(5)(iv) of this section, such person shall submit in connection with his request results of the tests and assay listed after each of the following make by him on an accurately representative sample of:

(a) The batch: average potency per tablet, average moisture, disintegration time if it is chlortetracycline hydrochloride or tetracycline tablets, and dissolution if it is tetracycline hydrochloride tablets.

(b) The chlortetracycline, tetracycline hydrochloride, tetracycline, or tetracycline phosphate complex used in making the batch: Potency, moisture, pH, crystallinity, absorptivity (if it is tetracycline hydrochloride, tetracycline, or tetracycline phosphate complex) and identity if it is tetracycline phosphate complex.

(iii) Except as otherwise provided by paragraph (a)(5)(iv) of this section, such person shall submit in connection with his request, in the quantities hereinafter indicated, accurately representative samples of the following:

(a) The batch: one tablet for each 5,000 tablets in the batch, but in no case less than 30 tablets, collected by taking single tablets at such intervals throughout the entire time of prepara-

tion that the quantities compressed during the intervals are approximately equal.

(b) The chlortetracycline, tetracycline hydrochloride, tetracycline, or tetracycline phosphate complex used in making the batch: 10 packages, each containing approximately equal portions of not less than 60 milligrams, and if it is tetracycline phosphate complex, one additional package containing approximately 1 gram. Each such package shall be packaged in accordance with the requirements of § 510.45 of this chapter.

(c) In case of an initial request for certification, each other ingredient used in making the batch; one package of each containing approximately 5 grams.

(iv) No result referred to in paragraph (a)(5)(ii)(b) of this section and no sample referred to in paragraph (a)(5)(iii)(b) of this section are required if such result or sample has been previously submitted.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Place a representative number of tablets into a high-speed glass blender jar containing sufficient 0.1N hydrochloric acid for chlortetracycline assay or 0.1N hydrochloric acid for tetracycline assay to obtain a stock solution of convenient concentration. Blend for 3 to 5 minutes. Remove an aliquot of the stock solution and further dilute with sterile distilled water to the reference concentration of 0.06 microgram of chlortetracycline hydrochloride per milliliter (estimated) or 0.24 microgram of tetracycline hydrochloride per milliliter (estimated).

(2) *Moisture.* Proceed as directed in § 436.200(b) or § 436.201 of this chapter. If it is tetracycline hydrochloride tablets and stability data have been submitted to prove that the drug is stable when it contains not more than 6 percent moisture, use the method described in § 436.201 of this chapter and proceed as directed in § 436.201(e)(3) of this chapter.

(3) *Disintegration time.* Proceed as directed in § 436.212 of this chapter.

(4) *Dissolution.* Proceed as directed in § 436.215 of this chapter, except in

lieu of paragraph (a) of that section, distance of 4.5 ± 0.5 centimeters should be maintained between the lower edge of the stirring blade and the lower inner surface of the vessel during the test. The quantity Q (the amount of tetracycline hydrochloride dissolved) is 60 percent within 30 minutes and 80 percent within 60 minutes.

(c) *Conditions of marketing*—(1) *Specifications.* Meets the requirements of paragraphs (a) and (b) of this section.

(2) *Sponsors.* (i) See No. 000010 in § 510.600(c) of this chapter for use of the 250-milligram chlortetracycline hydrochloride bolus.

(ii) See No. 010042 in § 510.600(c) of this chapter for use of the 25-milligram tablet and the 500-milligram bolus.

(3) *Special considerations.* The quantities of antibiotic in paragraph (c)(6) of this section refer to the activity of the master standard.

(4) *Related tolerances.* See § 556.150 of this chapter.

(5) *NAS/NRC status.* The conditions of use specified in paragraph (c)(6) of this section are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified in § 514.111 of this chapter but may require bioequivalency and safety information.

(6) *Conditions of use.* Administer orally as chlortetracycline hydrochloride tablets or boluses to calves as follows:

(i) *Amount.* 250 milligrams per bolus.

(a) *Indications for use.* Treatment of bacterial enteritis (scours) caused by *E. coli* and bacterial pneumonia associated with *Pasteurella* spp., *Klebsiella* spp., and *Hemophilus* spp.

(b) *Limitations.* Administer 1 bolus (250 milligrams) per 50 pounds of body weight twice a day for 3 to 5 days; administer bolus directly by mouth or crush and dissolve in milk or water for drenching or bucket feeding; if no improvement is noted after 3 days of treatment, consult a veterinarian; do not use for more than 5 days; do not administer within 24 hours of slaughter.

(ii) *Amount.* 25 milligrams per tablet.

(a) *Indications for use.* Control and treatment of bacterial enteritis

(scours) caused by *E. coli* and *Salmonella* spp. and bacterial pneumonia associated with *Pasteurella* spp., *Hemophilus* spp., and *Klebsiella* spp., susceptible to chlortetracycline.

(b) *Limitations.* Administer 1 tablet (25 milligrams) for each 5 pounds of body weight every 12 hours daily for 3 to 5 days; administer tablet directly by mouth or crush and dissolve in water for drenching; if no improvement is noted after 3 days of treatment, consult a veterinarian; do not use for more than 5 days; when feeding milk or milk replacer, administration 1 hour before or 2 hours after feeding is recommended; do not administer within 24 hours of slaughter.

(iii) *Amount.* 500 milligrams per bolus.

(a) *Indications for use.* Treatment of bacterial enteritis (scours) caused by *E. coli* and *Salmonella* spp. and bacterial pneumonia associated with *Pasteurella* spp., *Hemophilus* spp., and *Klebsiella* spp., susceptible to chlortetracycline.

(b) *Limitations.* Administer 1 bolus (500 milligrams) per 100 pounds of body weight twice a day for 3 to 5 days; administer directly by mouth or crush and dissolve in water for drenching; if no improvement is noted after 3 days of treatment, consult a veterinarian; do not use for more than 5 days; do not administer within 24 hours of slaughter.

(Secs. 507, 512, 59 Stat. 463 as amended; secs. 521 (i) and (n), 572, 82 Stat. 343-351 (21 U.S.C. 357, 360b); secs. 507, 512(n), 701 (f) and (g), 52 Stat. 1055-1056, as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371 (f) and (g)))

(40 FR 13924, Mar. 27, 1975, as amended at 43 FR 11179, Mar. 17, 1978; 43 FR 14647, Apr. 7, 1978; 44 FR 48190, Aug. 17, 1979; 47 FR 32938, July 30, 1982; 48 FR 51294, Nov. 8, 1983; 49 FR 4374, Feb. 6, 1984; 49 FR 37058, Sept. 21, 1984; 50 FR 19922, May 13, 1985)

§§ 546.110e-546.110f [Reserved]

§ 546.110g Chlortetracycline hydrochloride in oil oral.

(a) *Requirements for certification—*
(1) *Standards of identity, strength, quality, and purity.* Chlortetracycline hydrochloride in oil oral is crystalline chlortetracycline hydrochloride in a

suitable and harmless vegetable oil base. It contains not less than 50 milligrams of chlortetracycline hydrochloride per milliliter. Its moisture content is not more than 1.0 percent. The chlortetracycline hydrochloride used conforms to the requirements of § 446.10a(a)(1) of this chapter. Each other ingredient used, if its name is recognized in the U.S.P. or N.F., conforms to the standards prescribed therefor by such official compendium.

(2) *Packaging.* The immediate containers shall be well closed or tight containers as defined by the U.S.P. They shall be of such composition as will not cause any change in the strength, quality, or purity of the contents beyond any limit therefor in applicable standards, except that minor changes so caused that are normal and unavoidable in good marketing, storage, and distribution practice shall be disregarded. Unless it is packaged for repacking, each such container shall be filled with a volume of chlortetracycline hydrochloride in oil in excess of that designated, which excess shall be sufficient to permit the withdrawal and the administration of the volume indicated, whether administered in single or multiple doses.

(3) *Labeling.* Each package shall bear on its label or labeling, as hereinafter indicated:

(i) On the outside wrapper or container and the immediate container of the package:

(a) The batch mark.

(b) The number of milligrams of chlortetracycline hydrochloride per milliliter.

(c) The statement "Expiration date _____", the blank being filled in with the date that is 24 months, 36 months, or 48 months after the month during which the batch was certified.

(d) The statement "For oral use in suckling pigs only."

(ii) On the circular or other labeling within or attached to the package, adequate directions and warnings for the veterinary use of such drug by the laity.

(4) *Request for certification; samples.* (i) In addition to complying with the requirements of § 514.50 of this chapter, a person who requests certification of a batch shall submit with his

request a statement showing the batch mark, the number of packages of each size in such batch, the batch mark and (unless it was previously submitted) the date on which the latest assay of the chlortetracycline hydrochloride used in making such batch was completed, the quantity of each ingredient used in making the batch, the date on which the latest assay of the drug was completed, and a statement that each component of the oil base used conforms to the requirements prescribed therefor by this section.

(ii) Except as otherwise provided by paragraph (a)(4)(iv) of this section, such person shall submit in connection with his request results of the tests and assays listed after each of the following, made by him on an accurately representative sample of:

(a) The batch: Potency and moisture.

(b) The chlortetracycline hydrochloride used in making the batch: Potency, moisture, pH, and crystallinity.

(iii) Except as otherwise provided by paragraph (a)(4)(iv) of this section, such person shall submit in connection with his request, in the quantities hereinafter indicated, accurately representative samples of the following:

(a) The batch: 1 package for each 5,000 packages in the batch, but in no case less than 5 packages, collected by taking single packages at such intervals throughout the entire time of packaging the batch that the quantities packaged during the intervals are approximately equal.

(b) The chlortetracycline used in making the batch: 10 packages, containing approximately equal portions of not less than 60 milligrams each, packaged in accordance with the requirements of § 510.45 of this chapter.

(c) In case of an initial request for certification, each other ingredient used in making the batch: 1 package of each component of the oil base, each containing approximately 200 grams.

(iv) No result referred to in paragraph (a)(4)(ii)(b) of this section, and no sample referred to in paragraph (a)(4)(iii)(b) of this section, is required if such result or sample has been previously submitted.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in

§ 446.510(b)(1) of this chapter. The potency is satisfactory if it contains not less than 85 percent of the number of milligrams of chlortetracycline hydrochloride that it is represented to contain.

(2) *Moisture.* Proceed as directed in § 436.500(c) of this chapter, using a weighed sample of approximately 1 gram dissolved in 10 milliliters of a mixture of equal parts of dry chloroform and carbon tetrachloride; but in lieu of calculating the milliliters of Karl Fischer reagent equivalent to 10 milliliters of chloroform, determine the milliliters of reagent equivalent to 10 milliliters of the mixture of chloroform and carbon tetrachloride.

(Secs. 507, 512, 59 Stat. 463 as amended; sec. 572, 82 Stat. 343-351 (21 U.S.C. 357, 360b))

[40 FR 13924, Mar. 27, 1975, as amended at 41 FR 10886, Mar. 15, 1976; 43 FR 11180, Mar. 17, 1978; 50 FR 19922, May 13, 1985]

§ 546.113 Chlortetracycline bisulfate oral dosage forms.

§ 546.113a Chlortetracycline bisulfate soluble powder.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Chlortetracycline bisulfate soluble powder is chlortetracycline bisulfate with or without sulfamethazine bisulfate and with or without one or more suitable and harmless colorings, buffer substances, and diluents. It contains the equivalent of 25.6 grams or 102.4 grams of chlortetracycline hydrochloride per pound of powder. If it contains 102.4 grams equivalent of chlortetracycline hydrochloride, it may also contain sulfamethazine bisulfate equivalent to 102.4 grams of sulfamethazine. The moisture content is not more than 2 percent. The chlortetracycline bisulfate used conforms to the requirements of § 539.210b of this chapter. Each other substance used, if its name is recognized in the U.S.P. or N.F., conforms to the standards prescribed therefor by such official compendium.

(2) *Packaging.* In all cases, the immediate container shall be a tight container as defined by the U.S.P. The composition of the immediate container shall be such as will not cause any

change in the strength, quality, or purity of the contents beyond any limits therefor in applicable standards, except that minor changes so caused that are normal and unavoidable in good packaging, storage, and distribution practice shall be disregarded.

(3) *Labeling.* Each package shall bear on its label or labeling, as herein after indicated, the following:

(i) On the outside wrapper or container and the immediate container:

(a) The batch mark.

(b) The number of grams of chlortetracycline hydrochloride equivalent per pound and, if it contains sulfamethazine bisulfate, the number of grams of sulfamethazine equivalent per pounds in the immediate container.

(c) The number of pounds of powder in each immediate container.

(d) [Reserved]

(e) The statement "Expiration date _____", the blank being filled in with the date that is 12 months after the month during which the batch was certified, except that the blank may be filled in with the date that is 24, 30, 36, 42, or 48 months after the month during which the batch was certified if the person who requests certification has submitted to the Commissioner results of tests and assays showing that after having been stored for such period of time such drug as prepared by him complies with the standards prescribed by paragraph (a)(1) of this section.

(ii) On the circular or other labeling within or attached to the package:

(a) Adequate directions and warnings for the veterinary use of such drug by the laity.

(b) If it is intended for use in animals raised for food production, labeling in accordance with the requirements of § 546.110c.

(4) *Request for certification; samples.*

(i) In addition to complying with the requirements of § 514.50 of this chapter, a person who requests certification of a batch shall submit with his request a statement showing the batch mark and (unless it was previously submitted) the date on which the latest assay of the chlortetracycline bisulfate used in making such batch was completed, the number of grams of

chlortetracycline hydrochloride equivalent per pound, the number of pounds of powder, the number of packages of each size in the batch, the quantity of each ingredient used in making the batch, the date on which the latest assay of the drug comprising such batch was completed, and a statement that each ingredient used in making the batch conforms to the requirements prescribed therefor, if any, by this section.

(ii) Except as otherwise provided in paragraph (a)(4)(iv) of this section, such person shall submit in connection with his request results of the tests and assays listed after each of the following, made by him on an accurately representative sample of:

(a) The batch: Potency and moisture.

(b) The chlortetracycline bisulfate used in making the batch: Potency, moisture, butyl alcohol content, sulfate content, absorptivity, and crystallinity.

(iii) Except as otherwise provided by paragraph (a)(4)(iv) of this section, such person shall submit in connection with his request, in the quantities hereinafter indicated, accurately representative samples of the following:

(a) The batch: One 1-ounce portion for each 5,000 immediate containers in the batch, but in no case less than five 1-ounce portions. Such sample shall be collected by taking single 1-ounce portions at such intervals throughout the entire time the containers are being filled that the quantities filled during the intervals are approximately equal.

(b) The chlortetracycline bisulfate used in making the batch: 10 packages, each containing approximately equal portions of not less than 0.5 gram, packaged in accordance with the requirements of § 539.210b(a) of this chapter.

(c) In case of an initial request for certification, each other ingredient used in making the batch: One package of each containing approximately 5 grams.

(iv) The result referred to in paragraph (a)(4)(ii)(b) of this section, and the sample referred to in paragraph (a)(4)(iii)(b) of this section are not required if such result or sample has been previously submitted.

§ 546.113b

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(b) *Tests and methods of assay*—(1) *Potency*. Using an accurately weighed sample of approximately 500 milligrams, proceed as directed in § 436.106 of this chapter, preparing the sample as follows: Dissolve the 500 milligrams to be tested in 0.01N HCl to make a stock solution of convenient concentration. Further dilute with sterile distilled water to the reference concentration of 0.06 microgram of chlortetracycline hydrochloride equivalent activity (estimated). Its potency is satisfactory if it contains not less than 85 percent and not more than 125 percent of the labeled potency.

(2) *Moisture*. Proceed as directed in § 436.200b of this chapter.

(Secs. 507, 512, 59 Stat. 463 as amended; sec. 572, 82 Stat. 343-351 (21 U.S.C. 357, 360b))

[40 FR 13924, Mar. 27, 1975, as amended at 41 FR 10886, Mar. 15, 1976; 43 FR 11180, Mar. 17, 1978; 50 FR 19922, May 13, 1985]

§ 546.113b Chlortetracycline bisulfate-sulfamethazine bisulfate soluble powder.

(a) *Requirements for certification*. The requirements for certification for chlortetracycline bisulfate-sulfamethazine bisulfate soluble powder are described under § 546.113a(a).

(b) *Tests and methods of assay*. The tests and methods of assay for chlortetracycline bisulfate-sulfamethazine bisulfate soluble powder are described under § 546.113a(b).

(c) *Conditions of marketing*—(1) *Chemical name*. Sulfamethazine: N-(4,6-Dimethyl-2-pyrimidinyl) sulfanilamide.

(2) *Specifications*. Meets the requirements of § 546.113a(a).

(3) *Sponsor*. See No. 010042 in § 510.600(c) of this chapter.

(4) *Special considerations*. The quantities of antibiotic in paragraph (c)(6) of this section refer to the activity of the master standard.

(5) *Related tolerances*. See §§ 556.150 and 556.670 of this chapter.

(6) *Conditions of use*. It is used in drinking water of swine as follows:

(i) *Amount*. 250 milligrams of chlortetracycline with 250 milligrams of sulfamethazine per gallon.

(ii) *Indications for use*. Prevention and treatment of bacterial enteritis; aid in the reduction of the incidence of cervical abscesses; aid in the main-

tenance of weight gains in the presence of bacterial enteritis and atrophic rhinitis.

(iii) *Limitations*. Not to be used for more than 28 consecutive days; withdraw 15 days before slaughter; as sole source of chlortetracycline and sulfonamide.

[40 FR 13924, Mar. 27, 1975, as amended at 43 FR 19385, May 5, 1978]

§ 546.180 Tetracycline oral dosage forms.

§ 546.180a Tetracycline hydrochloride capsules.

(a) *Requirements for certification*. The requirements for certification for tetracycline hydrochloride capsules are described under § 446.181e(a)(1), with the following exceptions:

(1) Standards of identity, strength, quality, and purity: It may contain one or more suitable sulfonamides and harmless vitamin substances.

(2) When it is packaged for dispensing and intended solely for veterinary use: Its label and labeling shall bear the statement "Warning—Not for use in animals which are raised for food production" and shall comply with all of the requirements prescribed by § 546.110d(a)(4) and § 201.105 of this chapter.

(b) *Tests and methods of assay*. The tests and methods of assay for tetracycline hydrochloride capsules are as described under § 446.181e(b) (1) and (2) of this chapter.

(c) *Conditions of marketing*—(1) *Specifications*. Tetracycline capsules conform to the standards of identity, strength, quality, and purity prescribed by paragraph (a) of this section.

(2) *Sponsor*. See § 510.600(c) of this chapter for identification of the sponsors as listed in paragraph (c)(5) of this section.

(3) *Special considerations*. The quantity of tetracycline in paragraph (c)(5) of this section refers to the activity of tetracycline hydrochloride.

(4) [Reserved]

(5) *Conditions of use*. It is used as tetracycline hydrochloride for dogs as follows:

(i) *Amount*. 250 milligrams per capsule.

(a) *Indications for use.* For treatment of infections caused by organisms sensitive to tetracycline hydrochloride, such as bacterial gastroenteritis due to *E. coli* and urinary tract infections due to *Staphylococcus spp.* and *E. coli*.

(b) *Limitations.* Administer orally 25 milligrams per pound of body weight per day given in divided doses every 6 hours; treatment should be continued until symptoms of the disease have subsided and the temperature is normal for 48 hours; not for use in animals which are raised for food production; Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(c) *Sponsor.* See No. 000069 in § 510.600(c) of this chapter.

(ii) *Amount.* 125, 250, or 500 milligrams per capsule.

(a) *Indications for use.* For treatment of infections caused by organisms sensitive to tetracycline hydrochloride, such as bacterial gastroenteritis due to *E. coli* and urinary tract infections due to *Staphylococcus spp.* and *E. coli*.

(b) *Limitations.* Administer orally 25 milligrams per pound of body weight per day given in divided doses every 6 hours; treatment should be continued until symptoms of the disease have subsided and the temperature is normal for 48 hours; not for use in animals which are raised for food production; Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(c) *Sponsor.* See Nos. 000009 and 000693 in § 510.600(c) of this chapter.

(iii) *Amount.* 50, 100, 250, or 500 milligrams per capsule.

(a) *Indications for use.* For treatment of infections caused by organisms sensitive to tetracycline hydrochloride, such as bacterial gastroenteritis due to *E. coli* and urinary tract infections due to *Staphylococcus spp.* and *E. coli*.

(b) *Limitations.* Administer orally 25 milligrams per pound of body weight per day given in divided doses every 6 hours; treatment should be continued until symptoms of the disease have subsided and the temperature is normal for 48 hours; not for use in ani-

mals which are raised for food production; Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(c) *Sponsor.* See No. 000115 in § 510.600(c) of this chapter.

(iv) *Amount.* 50, 100, 125, 250, or 500 milligrams per capsule.

(a) *Indications for use.* For treatment of infections caused by organisms sensitive to tetracycline hydrochloride, such as bacterial gastroenteritis due to *E. coli* and urinary tract infections due to *Staphylococcus spp.* and *E. coli*.

(b) *Limitations.* Administer orally 25 milligrams per pound of body weight per day given in divided doses every 6 hours; treatment should be continued until symptoms of the disease have subsided and the temperature is normal for 48 hours; not for use in animals which are raised for food production; Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(c) *Sponsor.* See No. 000172 in § 510.600(c) of this chapter.

(Secs. 507, 512, 59 Stat. 463 as amended; sec. 572, 82 Stat. 343-351 (21 U.S.C. 357, 360b))

[40 FR 13924, Mar. 27, 1975, as amended at 42 FR 10982, Feb. 25, 1977; 43 FR 11180, Mar. 17, 1978; 47 FR 31864, July 23, 1982; 48 FR 30615, July 5, 1983; 50 FR 41490, Oct. 11, 1985; 54 FR 11698, Mar. 22, 1989]

EFFECTIVE DATE NOTE: At 54 FR 11698, Mar. 22, 1989, paragraph (c)(5)(i)(c) was revised, effective April 3, 1989. For the convenience of the user, the superseded text follows:

§ 546.180a Tetracycline hydrochloride capsules.

• • • • •
(c) • • •
(5) • • •
(i) • • •

(c) *Sponsor.* See Nos. 000009, 000693, and 053501 in § 510.600(c) of this chapter.

• • • • •

§ 546.180b Tetracycline tablets.

(a) *Requirements for certification.* The requirements for certification for tetracycline tablets are described under § 546.110d(a).

(b) *Tests and methods of assay.* The tests and methods of assay for tetracy-

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cline tablets are described under § 546.110d(b).

(c) *Conditions of marketing*—(1) *Specifications*. Tablets contain tetracycline as tetracycline hydrochloride.

(2) [Reserved]

(3) *Conditions of use*. It is used in dogs as follows:

(i) *Sponsor*. (a) For 100, 250, or 500 milligrams per tablet, see No. 000069 in § 510.600(c) of this chapter.

(b) For 250 milligrams per tablet, see No. 000009 in § 510.600(c) of this chapter.

(ii) *Indications for use*. For treatment of infections caused by organisms sensitive to tetracycline hydrochloride, such as bacterial gastroenteritis due to *E. coli* and urinary tract infections due to *Staphylococcus spp.* and *E. coli*.

(iii) *Limitations*. Administer orally 25 milligrams per pound of body weight per day given in divided doses every 6 hours; treatment should be continued until symptoms of the disease have subsided and the temperature is normal for 48 hours; not for use in animals which are raised for food production; Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13924, Mar. 27, 1975, as amended at 40 FR 39858, Aug. 29, 1975; 48 FR 30615, July 5, 1983]

§ 546.180c Tetracycline boluses.

(a) *Requirements for certification*. The requirements for certification for tetracycline boluses are described under § 546.110d(a).

(b) *Tests and methods of assay*. The tests and methods of assay for tetracycline boluses are described under § 546.110d(b).

(c) *Conditions of marketing*—(1) *Specifications*. Tetracycline boluses conform to the standards of identity, strength, quality, and purity prescribed by § 546.110d.

(2) *Sponsors*. See drug labeler codes in § 510.600(c) of this chapter for identity of sponsors as follows:

(i) No. 010042 for use of 500-milligram boluses as in paragraph (c)(6)(i) of this section.

(ii) No. 000009 for use of 500-milligram boluses as in paragraph (c)(6)(ii) of this section.

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(3) *Special considerations*. The quantity of tetracycline in paragraph (c)(2) (i) and (ii) of this section refers to the activity of tetracycline hydrochloride.

(4) *Related tolerances*. See § 550.720 of this chapter.

(5) *NAS/NRC status*. The conditions of use specified in paragraph (c)(6)(i) of this section are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified in § 514.111 of this chapter, but may require bioequivalency and safety information.

(6) *Conditions of use*. It is used as tetracycline hydrochloride in calves as follows:

(i) *Amount*. 10 milligrams per pound of body weight per day in divided doses.

(a) *Indications for use*. Control and treatment of bacterial enteritis (scours) caused by *E. coli* and bacterial pneumonia caused by *Pasteurella spp.*, *Hemophilus spp.*, and *Klebsiella spp.*

(b) *Limitations*. Administer orally for 3 to 5 days; do not slaughter animals for food within 14 days of treatment; use as sole source of tetracycline.

(ii) *Amount*. 10 milligrams per pound of body weight per day divided into two daily doses.

(a) *Indications for use*. Treatment of bacterial pneumonia caused by organisms susceptible to tetracycline and bacterial enteritis caused by *E. coli* and salmonella organisms susceptible to tetracycline.

(b) *Limitations*. Administer orally for not more than 5 days; do not slaughter animals for food within 12 days of treatment; use as sole source of tetracycline.

[47 FR 4680, Feb. 2, 1982, as amended at 47 FR 20111, May 11, 1982; 49 FR 1340, Jan. 11, 1984]

§ 546.180d Tetracycline soluble powder.

(a) *Requirements for certification*. The requirements for certification for tetracycline soluble powder are described under § 546.110c(a).

(b) *Tests and methods of assay*. The tests and methods of assay for tetracycline soluble powder are described under § 546.110c(b).

(c) *Conditions of marketing*—(1) *Specifications*. Tetracycline soluble powder conforms to the standards of identity, strength, quality, and purity prescribed by § 546.110c.

(2) *Sponsor*. See § 510.600(c) of this chapter for identification of the sponsors as listed in paragraph (c)(6) of this section.

(3) *Special considerations*. The quantity of tetracycline in paragraph (c)(6) of this section refers to the activity of tetracycline hydrochloride.

(4) *Related tolerances*. See § 556.720 of this chapter.

(5) *NAS/NRC status*. The conditions of use specified in paragraphs (c)(6)(i)(c)(1), (iii)(d)(1), and (iv)(c)(1) of this section are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified in § 514.111 of this chapter, but may require bioequivalency and safety information.

(6) *Conditions of use*. (i) It is used as tetracycline hydrochloride in drinking water for calves as follows:

(a) *Amount*. 100 to 200 milligrams per gallon.

(1) *Indications for use*. As an aid in prevention of bacterial diarrhea, bacterial pneumonia, and shipping fever (hemorrhagic septicemia).

(2) *Limitations*. Administer for not more than 5 days; do not slaughter animals for food purposes within 5 days of treatment; prepare a fresh solution daily; as sole source of tetracycline.

(3) *Sponsor*. See Nos. 000009 and 000069 in § 510.600(c) of this chapter.

(b) *Amount*. 200 to 400 milligrams per gallon.

(1) *Indications for use*. For treatment of bacterial diarrhea, bacterial pneumonia, and shipping fever (hemorrhagic septicemia).

(2) *Limitations*. Administer for not more than 5 days; do not slaughter animals for food purposes within 5 days of treatment; prepare fresh solution daily; as sole source of tetracycline.

(3) *Sponsor*. See Nos. 000009 and 000069 in § 510.600(c) of this chapter.

(c) *Amount*. 10 milligrams per pound body weight daily.

(1) *Indications for use*. For the control and treatment of bacterial enteri-

tis (scours) caused by *Escherichia coli* and bacterial pneumonia (shipping fever complex) associated with *Pasteurella* spp., *Hemophilus* spp., and *Klebsiella* spp., susceptible to tetracycline.

(2) *Limitations*. Administer for 3 to 5 days; do not slaughter animals for food purposes within 5 days of treatment; use as sole source of tetracycline.

(3) *Sponsor*. See No. 054273 in § 510.600(c) of this chapter.

(ii) It is used as tetracycline hydrochloride in water or milk for newborn pigs as follows:

(a) *Amount*. 52 milligrams per day.

(b) *Indications for use*. For treatment of bacterial enteritis and bacterial pneumonia.

(c) *Limitations*. Administer for not more than 3 days; do not slaughter animals for food purposes within 4 days of treatment; prepare a fresh solution daily; as sole source of tetracycline.

(d) *Sponsor*. See Nos. 000009 and 000069 in § 510.600(c) of this chapter.

(iii) It is used as tetracycline hydrochloride in drinking water for swine as follows:

(a) *Amount*. 100 to 200 milligrams per gallon.

(1) *Indications for use*. As an aid in prevention of bacterial enteritis.

(2) *Limitations*. Do not slaughter animals for food purposes within 4 days of treatment; prepare a fresh solution daily; as sole source of tetracycline.

(3) *Sponsor*. See Nos. 000009 and 000069 in § 510.600(c) of this chapter.

(b) *Amount*. 200 to 400 milligrams per gallon.

(1) *Indications for use*. As an aid in prevention of bacterial pneumonia; for treatment of bacterial enteritis.

(2) *Limitations*. Do not slaughter animals for food purposes within 4 days of treatment; prepare a fresh solution daily; as sole source of tetracycline.

(3) *Sponsor*. See Nos. 000009 and 000069 in § 510.600(c) of this chapter.

(c) *Amount*. 400 milligrams per gallon.

(1) *Indications for use*. For treatment of bacterial pneumonia.

(2) *Limitations.* Do not slaughter animals for food purpose within 4 days of treatment; prepare a fresh solution daily; as sole source of tetracycline.

(3) *Sponsor.* See Nos. 000009 and 000069 in § 510.600(c) of this chapter.

(d) *Amount.* 10 milligrams per pound body weight daily.

(1) *Indications for use.* For the control and treatment of bacterial enteritis (scours) caused by *Escherichia coli* and bacterial pneumonia associated with *Pasteurella* spp., *Hemophilus* spp., and *Klebsiella* spp., susceptible to tetracycline.

(2) *Limitations.* Administer for 3 to 5 days; do not slaughter animals for food purposes within 4 days of treatment; use as sole source of tetracycline.

(3) *Sponsor.* See No. 054273 in § 510.600(c) of this chapter.

(iv) It is used as tetracycline hydrochloride in drinking water for turkeys and chickens as follows:

(a) *Amount.* 100 to 200 milligrams per gallon.

(1) *Indications for use.* As an aid in prevention of chronic respiratory disease (air-sac infection), hexamitiasis, blue comb (nonspecific enteritis), infectious sinusitis, and synovitis.

(2) *Limitations.* Administer for not more than 21 days; do not slaughter birds for food within 4 days of treatment; not for use in chickens and turkeys producing eggs for human consumption; prepare fresh solution daily; as sole source of tetracycline.

(3) *Sponsor.* See Nos. 000009 and 000069 in § 510.600(c) of this chapter.

(b) *Amount.* 200 to 400 milligrams per gallon.

(1) *Indications for use.* For treatment of chronic respiratory disease (air-sac infection), hexamitiasis, blue comb (non-specific enteritis), infectious sinusitis, and synovitis.

(2) *Limitations.* Administer for not more than 21 days; do not slaughter birds for food within 4 days of treatment; not for use in chickens and turkeys producing eggs for human consumption; prepare a fresh solution daily; as sole source of tetracycline.

(3) *Sponsor.* See Nos. 000009 and 000069 in § 510.600(c) of this chapter.

(c) *Amount.* 1,000 milligrams per gallon.

(1) *Indications for use.* Chickens: For control of chronic respiratory disease and air sac infection caused by *Mycoplasma gallisepticum* and *Escherichia coli*; infectious synovitis caused by *M. synoviae* susceptible to tetracycline. Turkeys: For control of infectious synovitis caused by *M. synoviae* and bluecomb (transmissible enteritis, coronaviral enteritis) caused by complicating bacterial organisms susceptible to tetracycline.

(2) *Limitations.* Administer medicated drinking water to chickens and turkeys to provide a dose of 25 milligrams per pound of body weight daily; administer for not more than 14 consecutive days; do not slaughter birds for food within 4 days of treatment; not for use in chickens and turkeys producing eggs for human consumption; prepare a fresh solution daily; use as sole source of tetracycline.

(3) *Sponsor.* See No. 054273 in § 510.600(c) of this chapter.

[40 FR 13924, Mar. 27, 1975, as amended 49 FR 47467, Dec. 5, 1984; 51 FR 4461, Dec. 10, 1986; 53 FR 40728, Oct. 18, 1988]

§ 546.180e Tetracycline oral liquid.

(a) *Requirements for certification.*
(1) *Standards of identity, strength, quality, and purity.* Tetracycline oral liquid is a suspension composed of tetracycline with or without one or more suitable and harmless buffer substances, suspending and stabilizing agents, and preservatives suspended in a suitable and harmless vehicle. Each milliliter contains the equivalent of either 25 or 100 milligrams of tetracycline hydrochloride. It contains not less than 90 percent and not more than 120 percent of the labeled amount of tetracycline hydrochloride. Its pH is not less than 3.5 nor more than 6.0. The tetracycline used conforms to the standards prescribed by § 446.80(a)(1) of this chapter.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 510.55 of this chapter and paragraph (c) of this section.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assay on:

(a) The tetracycline used in making the batch for potency, moisture, pH, absorptivity, 4-epian hydrotetracycline content, crystallinity, and identity.

(b) The batch for potency and pH.

(ii) Samples required:

(a) The tetracycline used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch: A minimum of 10 immediate containers.

(b) *Tests and methods of assay*—(1) *Potency*. Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Transfer an accurately measured representative portion of the well-shake suspension to an appropriate-size volumetric flask and dilute to volume with 0.1N hydrochloric acid to give a stock solution of convenient concentration containing not less than 150 micrograms of tetracycline hydrochloride per milliliter (estimated). Mix well. Remove an aliquot of the stock solution and further dilute with sterile distilled water to the reference concentration of 0.24 microgram of tetracycline hydrochloride per milliliter (estimated).

(2) *pH*. Proceed as directed in § 436.202 of this chapter, using the undiluted suspension.

(c) *Conditions of marketing*—(1) *Specifications*. Tetracycline oral liquid conforms to the standards of identity, strength, quality, and purity prescribed by paragraph (a) of this section.

(2) *Sponsor*. See § 510.600(c) of this chapter for identification of the sponsors as listed in paragraph (c)(5) of this section.

(3) *Special considerations*. The quantity of tetracycline in paragraph (c)(5) of this section refers to the activity of tetracycline hydrochloride.

(4) [Reserved]

(5) *Conditions of use*. It is used as tetracycline as follows:

(i) *Dogs*—(a) *Amount*. 25 or 100 milligrams per milliliter.¹

(b) *Indications for use*. For treatment of infections caused by organisms sensitive to tetracycline hydrochloride, such as bacterial gastroenteritis due to *E. coli* and urinary tract infections due to *Staphylococcus spp.* and *E. coli*.¹

(c) *Limitations*. Administer orally 25 milligrams per pound of body weight per day given in divided doses every 6 hours; treatment should be continued until symptoms have subsided and the temperature is normal for 48 hours; not for use in animals which are raised for food production; Federal law restricts this drug to use by or on the order of a licensed veterinarian.¹

(d) *Sponsor*. See No. 000069 in § 510.600(c) of this chapter.

(ii) *Dogs and cats*—(a) *Amount*. 100 milligrams per milliliter.

(b) *Indications for use*. For treatment of infections caused by organisms susceptible to tetracycline hydrochloride, such as bacterial gastroenteritis due to *E. coli* and urinary tract infections due to *Staphylococcus spp.* and *E. coli*.

(c) *Limitations*. Administer orally 25 milligrams per pound of body weight per day given in divided doses every 6 hours; treatment should be continued until the temperature has been normal for 48 hours; not for use in food-producing animals; Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(d) *Sponsor*. See No. 000009 in § 510.600(c) of this chapter.

(Secs. 507, 512, 59 Stat. 463 as amended; sec. 572, 82 Stat. 343-351 (21 U.S.C. 357, 360b))

(40 FR 13924, Mar. 27, 1975, as amended at 43 FR 11180, Mar. 17, 1978; 43 FR 14647, Apr. 7, 1978; 48 FR 30615, July 5, 1983; 50 FR 19922, May 13, 1985)

§ 546.180f Tetracycline oral suspension.

(a) *Requirements for certification*—(1) The requirements for certification for tetracycline hydrochloride oral suspension (tetracycline hydrochloride homogenized mixture); tetracycline phosphate complex oral suspension (tetracycline phosphate complex oral drops); tetracycline hydrochloride oral solution; tetracycline calcium oral suspension; tetracycline oral suspension

¹ These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

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are described under § 446.180c of this chapter.

(2) When it is packaged for dispensing and intended solely for veterinary use, its label and labeling shall comply with all the requirements prescribed by § 446.180c(a)(3) of this chapter, except that in lieu of the statement, "Caution: Federal law prohibits dispensing without prescription," each package shall include information containing directions and warnings adequate for the veterinary use of the drug by the laity and the statement, "Warning—Not for use in animals which are raised for food production."

(b) *Tests and methods of assay.* The tests and methods of assay for tetracycline hydrochloride oral suspension (tetracycline hydrochloride homogenized mixture); tetracycline phosphate complex oral suspension (tetracycline phosphate complex oral drops); tetracycline hydrochloride oral solution; tetracycline calcium oral suspension; tetracycline oral suspension are described under § 446.180c of this chapter.

§ 546.180g Tetracycline phosphate complex and sodium novobiocin capsules.

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality, and purity.* The product is a gelatin capsule containing tetracycline phosphate complex and sodium novobiocin with or without one or more suitable and harmless lubricants and fillers. Each capsule contains the equivalent activity of 60 milligrams of tetracycline hydrochloride and 60 milligrams of novobiocin. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the labeled amount of tetracycline hydrochloride and novobiocin. Its loss on drying is not more than 9.0 percent. The tetracycline phosphate complex used conforms to the standards prescribed by § 446.82(a)(1) of this chapter. The sodium novobiocin used conforms to the standards prescribed by § 455.51(a) of this chapter.

(2) *Labeling.* It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the

requirements of § 514.50 of this chapter, each such request shall contain:

(i) *Results of tests and assays on:* (a) The tetracycline phosphate complex used in making the batch for potency, moisture, pH, absorptivity, crystallinity, and identity.

(b) The sodium novobiocin used in making the batch for potency, loss on drying, pH, residue on ignition, specific rotation, crystallinity, and identity.

(c) The batch for tetracycline hydrochloride content, novobiocin content, and loss on drying.

(ii) *Samples required:* (a) The tetracycline phosphate complex and sodium novobiocin used in making the batch: 10 packages each, each containing approximately 500 milligrams.

(b) The batch: A minimum of 80 capsules.

(b) *Tests and methods of assay—*(1) *Potency—*(i) *Tetracycline content.* Proceed as directed in § 436.106 of this chapter, except use test organism J in lieu of organism A and prepare the sample as follows: Place a representative number of capsules in a high-speed glass blender jar with sufficient 0.1 N hydrochloric acid to give a stock solution of convenient concentration. Blend 3 to 5 minutes. Further dilute an aliquot of stock solution with sterile distilled water to the reference concentration of 0.24 microgram of tetracycline hydrochloride per milliliter (estimated).

(ii) *Novobiocin content.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place a representative number of capsules in a high-speed blender jar containing 1.0 milliliter of polysorbate 80 and sufficient 0.1 M potassium phosphate buffer, pH 8.0 (solution 3), to obtain a stock solution of convenient concentration. Blend 3 to 5 minutes. Further dilute an aliquot of the stock solution with 10 percent potassium phosphate buffer, pH 6.0 (solution 6), to the reference concentration of 0.5 microgram of novobiocin per milliliter (estimated).

(2) *Loss on drying.* Proceed as directed in § 436.200(b) of this chapter.

(c) *Conditions of marketing—*(1) *Specifications.* Meets the requirements of paragraph (a) of this section.

(2) *Sponsor.* No. 000009 in § 510.600(c) of this chapter.

(3) *Special considerations.* The quantities of antibiotics refer to the activity of the antibiotic master standards.

(4) *Conditions of use.* It is used orally in dogs as follows:

(i) *Amount.* 10 milligrams of each per pound of body weight (1 capsule for each 6 pounds) every 12 hours.

(ii) *Indications for use.* It is used in treatment of acute or chronic canine respiratory infections such as tonsillitis, bronchitis, and tracheobronchitis when caused by pathogens susceptible to tetracycline and/or novobiocin, such as *Staphylococcus* spp. and *Escherichia coli*.

(iii) *Limitations.* Treatment should be continued for at least 48 hours after the temperature has returned to normal and all evidence of infection has disappeared. As with all antibiotics, appropriate in vitro culturing and susceptibility tests of samples taken before treatment should be conducted. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[42 FR 54801, Oct. 11, 1977, as amended at 50 FR 19922, May 13, 1985]

§ 546.180h Tetracycline hydrochloride and sodium novobiocin tablets.

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality, and purity.* The product is a tablet containing tetracycline hydrochloride and sodium novobiocin with one or more suitable binders, fillers, lubricants, expanders, and coloring agent. Each tablet contains the equivalent activity of 60 milligrams of tetracycline hydrochloride and 60 milligrams of novobiocins, or 180 milligrams of tetracycline hydrochloride and 180 milligrams of novobiocin. Its potency is satisfactory if it is not less than 90 percent and not more than 125 percent of the labeled amount of tetracycline hydrochloride and novobiocin. Its loss on drying is not more than 6.0 percent. The tablets disintegrate within 60 minutes. The tetracycline hydrochloride used conforms to the standards of § 446.81a(a)(1) of this chapter, except for sterility and depressor substances. The sodium novo-

biocin used conforms to the standards prescribed by § 455.51(a)(1) of this chapter.

(2) *Labeling.* It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) *Results of tests and assays on:* (a) The tetracycline hydrochloride used in making the batch for potency, loss on drying, pH, absorptivity, and identity;

(b) The sodium novobiocin used in making the batch for potency, loss on drying, pH, residue on ignition, specific rotation, crystallinity, and identity;

(c) The batch for tetracycline hydrochloride content, novobiocin content, loss on drying, and disintegration time.

(ii) *Samples required:* (a) The tetracycline hydrochloride and sodium novobiocin used in making the tablets: 10 packages each, each containing approximately 500 milligrams.

(b) The batch: A minimum of 80 tablets.

(b) *Tests and methods of assay—*(1)

Potency—(i) *Tetracycline content:* Proceed as directed in § 436.106 of this chapter, except use test organism J in lieu of organism A and prepare the sample as follows: Place a representative number of tablets in a high-speed glass blender jar with sufficient 0.1 N HCl to give a stock solution of convenient concentration. Blend 3 to 5 minutes. Further dilute an aliquot of the stock solution with sterile distilled water to the reference concentration of 0.24 microgram of tetracycline hydrochloride per milliliter (estimated).

(ii) *Novobiocin content:* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place a representative number of tablets in a high-speed glass blender jar with 1.0 milliliter of polysorbate 80 and sufficient 0.1 M potassium phosphate buffer, pH 8.0 (solution 3), to give a stock solution of convenient concentration. Blend 3 to 5 minutes. Further dilute an aliquot of the stock solution with 10 percent potassium phosphate buffer, pH 6.0 (solution 6),

to the reference concentration of 0.5 microgram of novobiocin per milliliter (estimated).

(2) *Loss on drying.* Proceed as directed in § 436.200(b) of this chapter.

(3) *Disintegration time.* Proceed as directed in § 436.212 of this chapter, using the procedure described in paragraph (e)(1) of that section.

(c) *Conditions of marketing—(1) Specifications.* Meets the requirements of paragraph (a) of this section.

(2) *Sponsor.* No. 000009 in § 510.600(c) of this chapter.

(3) *Special considerations.* The quantities of antibiotic refer to the activity of the antibiotic master standards.

(4) *Conditions of use.* It is used orally in dogs as follows:

(i) *Amount.* Ten milligrams of each per pound of body weight (1 single strength tablet for each 6 pounds or 1 triple strength tablet for each 18 pounds).

(ii) *Indications for use.* It is used in the treatment of acute or chronic canine respiratory infections such as tonsillitis, bronchitis, and tracheobronchitis when caused by pathogens susceptible to tetracycline and/or novobiocin, such as *Staphylococcus* spp. and *Escherichia coli*.

(iii) *Limitations.* Treatment should be continued for at least 48 hours after the temperature has returned to normal and all evidence of infection has disappeared. As with all antibiotics, appropriate in vitro culturing and susceptibility tests of samples taken before treatment should be conducted. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[42 FR 54801, Oct. 11, 1977; as amended at 42 FR 61256, Dec. 2, 1977; 50 FR 19922, May 13, 1985; 52 FR 43060, Nov. 9, 1987]

§ 546.180i Tetracycline hydrochloride, sodium novobiocin, and prednisolone tablets.

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality, and purity.* The product is a tablet containing tetracycline hydrochloride, sodium novobiocin, and prednisolone anhydrous with one or more suitable binders, fillers, lubricants, expanders, and coloring agents. Each

tablet contains the equivalent activity of 60 milligrams of tetracycline hydrochloride, 60 milligrams of novobiocin, and 1.5 milligrams of prednisolone or 180 milligrams of tetracycline hydrochloride, 180 milligrams of novobiocin, and 4.5 milligrams of prednisolone. Its potency is satisfactory if it is not less than 90 percent and not more than 125 percent of the labeled amount of tetracycline hydrochloride and novobiocin. Its loss on drying is not more than 6.0 percent. Its 4-epianhydrotetracycline content is not more than 2.0 percent. The tablets disintegrate within 60 minutes. The tetracycline hydrochloride used conforms to the standards of § 446.81(a)(1) of this chapter. The sodium novobiocin used conforms to the standards prescribed by § 455.51(a)(1) of this chapter.

(2) *Labeling.* It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) *Results of tests and assays on:* (a) The tetracycline hydrochloride used in making the batch for potency, loss on drying, pH, absorptivity, 4-epianhydrotetracycline content, and identity;

(b) The sodium novobiocin used in making the batch for potency, loss on drying, pH, residue on ignition, specific rotation, crystallinity, and identity.

(c) The batch for tetracycline hydrochloride content, novobiocin content, loss on drying, 4-epianhydrotetracycline content, and disintegration time.

(ii) *Samples required:* (a) The tetracycline hydrochloride and sodium novobiocin used in making the tablets: 10 packages each, each containing approximately 500 milligrams.

(b) The batch: A minimum of 80 tablets.

(b) *Tests and methods of assay—(1) Potency—(i) Tetracycline content.* Proceed as directed in § 436.106 of this chapter, except use test organism J in lieu of organism A and prepare the sample as follows: Place a representative number of tablets in a high-speed glass blender jar with sufficient 0.1N HCl to give a stock solution of convenient concentration. Blend 3 to 5 min-

utes. Further dilute an aliquot of the stock solution with sterile distilled water to the reference concentration of 0.24 microgram of tetracycline hydrochloride per milliliter (estimated).

(ii) *Novobiocin content*. Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place a representative number of tablets in a high-speed glass blender jar with 1.0 milliliter of polysorbate 80 and sufficient 0.1M potassium phosphate buffer, pH 8.0 (solution 3), to give a stock solution of convenient concentration. Blend 3 to 5 minutes. Further dilute an aliquot of the stock solution with 10 percent potassium phosphate buffer, pH 6.0 (solution 6), to the reference concentration of 0.5 microgram of novobiocin per milliliter (estimated).

(2) *Loss on drying*. Proceed as directed in § 436.200(b) of this chapter.

(3) *4-Epianhydrotetracycline content*. Proceed as directed in § 436.309 of this chapter.

(4) *Disintegration time*. Proceed as directed in § 436.212 of this chapter, using the procedure described in paragraph (e)(1) of that section.

(c) *Conditions of marketing—(1) Specifications*. Meets the requirement of paragraph (a) of this section.

(2) *Sponsor*. See No. 000009 in § 510.600(c) of this chapter.

(3) *Special considerations*. The quantities of antibiotic refer to the activity of the antibiotic master standards.

(4) *Conditions of use*. It is used orally in dogs as follows:

(i) *Amount*. Ten milligrams of each antibiotic and 0.25 milligram of prednisolone per pound of body weight (1 single-strength tablet for each 6 pounds or 1 triple-strength tablet for each 18 pounds) every 12 hours for 48 hours. Treatment is to be continued with novobiocin and tetracycline alone at the same dose schedule for an additional 3 days or longer as needed.

(ii) *Indications for use*. It is used in the treatment of acute and chronic canine respiratory infections such as tonsillitis, bronchitis, and tracheobronchitis when caused by pathogens susceptible to tetracycline and/or novobiocin, such as *Staphylococcus spp.* and *Escherichia coli*, when it is neces-

sary to initially reduce the severity of associated clinical signs.

(iii) *Limitations*. As with all antibiotics, appropriate in vitro culturing and susceptibility tests of samples taken before treatment should be conducted. Administer only for the first 48 hours of treatment. The product is contraindicated in animals with tuberculosis, hyperadrenocorticalism, or peptic ulcers. Clinical and experimental data have demonstrated that corticosteroids administered orally or parenterally to animals may induce the first stage of parturition when administered during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[46 FR 25086, May 5, 1981, as amended at 50 FR 19922, May 13, 1985; 52 FR 43061, Nov. 9, 1987]

Subpart B—[Reserved]

Subpart C—Ophthalmic and Topical Dosage Forms

§ 546.312 Chlortetracycline/tetracycline ophthalmic and topical dosage forms.

§ 546.312a Chlortetracycline-neomycin-streptomycin/dihydrostreptomycin ointment; tetracycline hydrochloride-neomycin-streptomycin/dihydrostreptomycin ointment.

(a) *Requirements for certification—*
(1) Chlortetracycline-neomycin-streptomycin ointment, chlortetracycline-neomycin-dihydrostreptomycin ointment, tetracycline hydrochloride-neomycin-streptomycin ointment, and tetracycline hydrochloride-neomycin-dihydrostreptomycin ointment conform to all requirements and are subject to all procedures prescribed by § 446.510a(a) of this chapter for chlortetracycline hydrochloride ointment and tetracycline hydrochloride ointment, except that:

(i) They contain not less than 28 milligrams of chlortetracycline hydrochloride or tetracycline hydrochloride per gram.

(ii) They contain not less than 14 milligrams of neomycin per gram. The neomycin used conforms to the standards prescribed by § 444.42(a)(1) (i), (v), and (vi) of this chapter.

(iii) They contain not less than 14 milligrams of streptomycin or dihydrostreptomycin per gram. The streptomycin used conforms to the standards prescribed by § 444.70a(a)(1) of this chapter, except for sterility, pyrogens, and depressor substances. The dihydrostreptomycin used conforms to the standards prescribed by § 444.10a(a) of this chapter, except the standards for sterility, pyrogens, and depressor substances.

(2) Its expiration date shall be 36 months after the month during which the batch was certified.

(3) In addition to complying with the requirements of § 446.510a(a)(4) of this chapter, a person who requests certification of a batch shall submit with his request a statement showing the batch marks and (unless they were previously submitted) the results and dates of the latest tests and assays of the neomycin and streptomycin or dihydrostreptomycin used in making the batch for potency, moisture, pH, streptomycin content of the dihydrostreptomycin and crystallinity if it is crystalline dihydrostreptomycin. He shall also submit in connection with his request a sample consisting of not less than 8 packages of such ointment and (unless they were previously submitted) accurately representative samples of the following, in the quantities indicated:

(i) The neomycin used in making the batch; 5 packages, each containing approximately equal portions of not less than 0.5 gram.

(ii) The streptomycin or dihydrostreptomycin used in making the batch; 6 packages, each containing approximately equal portions of not less than 0.5 gram.

(b) *Tests and methods of assay*—(1) *Potency*—(i) *Chlortetracycline content*. Proceed as directed in § 446.10a(b)(1)(viii) of this chapter, except prepare the sample by one of the following methods: Place an accurately weighed sample of approximately 1 gram in an extraction funnel prepared by fusing a ground-glass joint to

the top of a medium-porosity sintered-glass filter funnel (30-millimeter diameter). Wash with five 10-milliliter portions of warm iso-octane and draw off the ointment base under vacuum. Discard the iso-octane washings. Wash the residue in the funnel four times with 10-milliliter portions of 0.3 percent piperidine in acetone solution. Withdraw each washing under vacuum. Combine the four washings in a 100-milliliter volumetric flask and make to mark with 0.1 M potassium phosphate buffer, pH 4.5. The solution for assay may also be prepared by placing a representative portion of the sample (usually 1.0 gram, accurately weighed) in a glass blending jar containing 199 milliliters of 0.01 N HCl and 1 milliliter of polysorbate 80. Using a high-speed blender, blend the mixture for 2 to 3 minutes and make proper estimated dilutions using 0.1 M potassium phosphate buffer, pH 4.5. Its content of chlortetracycline is satisfactory if it contains not less than 85 percent of the number of milligrams per gram of ointment that it is represented to contain.

(ii) *Tetracycline hydrochloride content*. Prepare the sample as directed in paragraph (b)(1)(i) of this section and proceed as directed in § 446.81a(b) of this chapter. Its content of tetracycline hydrochloride is satisfactory if it contains not less than 85 percent of the number of milligrams per gram of ointment that it is represented to contain.

(iii) *Neomycin content*. The residue remaining in the funnel after the extraction described in paragraph (b)(1)(i) of this section contains the neomycin and streptomycin or dihydrostreptomycin. Wash this residue five times, using 10-milliliter aliquots of 0.1 M potassium phosphate buffer, pH 8.0, drawing each washing off under vacuum. Combine the washings in a 100-milliliter volumetric flask and make to mark with 0.1 M potassium phosphate buffer, pH 8.0. Using an aliquot of this aqueous solution, proceed as directed in § 436.105 of this chapter. If *Staphylococcus epidermidis* is used as the test organism, proceed as directed in § 448.510d(b)(1)(ii) of this chapter. The content of neomycin is satisfactory if it contains not less than 85

percent of the number of milligrams per gram of ointment that it is represented to contain.

(iv) *Streptomycin content.* Using an aliquot of the aqueous solution prepared as directed in paragraph (b)(1)(iii) of this section, proceed as directed in § 444.70a(b)(1)(i) through (ix) of this chapter. The content of streptomycin is satisfactory if it contains not less than 85 percent of the number of milligrams per gram of ointment that it is represented to contain.

(v) *Dihydrostreptomycin content.* Using an aliquot of the aqueous solution prepared as directed in paragraph (b)(1)(iii) of this section, and the dihydrostreptomycin working standard as the standard of comparison, proceed as directed in § 444.70a(b)(1)(i) through (ix) of this chapter. The content of dihydrostreptomycin is satisfactory if it contains not less than 85 percent of the number of milligrams per gram of ointment that it is represented to contain.

(2) *Moisture.* Proceed as directed in § 540.380a(b)(2) of this chapter.

(Secs. 507, 512(n), 701(f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371(f) and (g)))

[40 FR 13924, Mar. 27, 1975, as amended at 46 FR 60569, Dec. 11, 1981; 50 FR 19922, May 13, 1985]

§ 546.312b Chlortetracycline/chlortetracycline hydrochloride/tetracycline hydrochloride ophthalmic.

(a) *Requirements for certification.* (1) The requirements for certification for chlortetracycline ophthalmic (chlortetracycline hydrochloride ophthalmic); tetracycline hydrochloride ophthalmic are described under § 446.310a of this chapter.

(2) When it is packaged for dispensing and intended solely for veterinary use, its label and labeling shall comply with all the requirements prescribed by § 446.310a(a)(3) of this chapter, except that in lieu of the statement "Caution: Federal law prohibits dispensing without prescription," each package shall include information containing directions and warnings adequate for the veterinary use of the drug by the laity.

(b) *Tests and methods of assay.* The tests and methods of assay for chlortetracycline ophthalmic (chlortetracycline hydrochloride ophthalmic); tetracycline hydrochloride ophthalmic are described under § 446.310a of this chapter.

§ 546.381 Tetracycline hydrochloride ophthalmic and topical dosage forms.

§ 546.381a Tetracycline hydrochloride-neomycin topical spray ointment.

(a) *Requirements for certification.* (1) The requirements for certification for tetracycline hydrochloride-neomycin spray topical ointment are described under § 446.581a of this chapter.

(2) When it is packaged for dispensing and intended solely for veterinary use, its label and labeling shall comply with all the requirements prescribed by § 446.581a(a)(3) of this chapter, except that in lieu of the statement "Caution: Federal law prohibits dispensing without prescription," each package shall include information containing directions adequate for the veterinary use of the drug by the laity.

(b) *Tests and methods of assay.* The tests and methods of assay for tetracycline hydrochloride-neomycin spray topical ointment are described under § 446.581a of this chapter.

§ 546.381b Tetracycline hydrochloride-neomycin in oil suspension.

(a) *Requirements for certification.* The requirements for certification for tetracycline hydrochloride-neomycin in oil suspension are described under § 446.581b of this chapter, except, if it is intended solely for veterinary use, it may contain one or more suitable fungicides and miticides. If it contains such ingredients, the labeling shall bear the name and quantity of each contained in each milliliter.

(b) *Tests and methods of assay.* The tests and methods of assay for tetracycline hydrochloride-neomycin in oil suspension are described under § 446.581b(b) of this chapter, except, if it is intended solely for veterinary use, it may contain one or more suitable fungicides and miticides. If it contains such ingredients, the labeling shall

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bear the name and quantity of each contained in each milliliter.

Subparts D—F [Reserved]

Subpart G—Rectal Dosage Forms

§ 546.713 Chlortetracycline/chlortetracycline hydrochloride/tetracycline hydrochloride suppositories.

(a) *Requirements for certification.*

(1) The requirements for certification for chlortetracycline suppositories (chlortetracycline hydrochloride suppositories); tetracycline hydrochloride suppositories are described under § 446.610 of this chapter.

(2) When it is packaged for dispensing and intended solely for veterinary use, its label and labeling shall comply with all the requirements prescribed by § 446.610(a)(3) of this chapter, except that in lieu of the statement, "Caution: Federal law prohibits dispensing without prescription", each package shall include information containing directions and warnings adequate for the veterinary use of the drug by the laity and the statement, "Warning—Not for use in animals which are raised for food production."

(b) *Tests and methods of assay.* The tests and methods of assay for chlortetracycline suppositories (chlortetracycline hydrochloride suppositories); tetracycline hydrochloride suppositories are described under § 446.610 of this chapter.

[40 FR 13924, Mar. 27, 1975, as amended at 41 FR 10886, Mar. 15, 1976]

PART 548—CERTIFIABLE PEPTIDE ANTIBIOTIC DRUGS FOR ANIMAL USE

Subpart A—Oral Dosage Forms

Sec.

548.112 Bacitracin methylene disalicylate oral dosage forms.

548.112a Soluble bacitracin methylene disalicylate.

548.112b Bacitracin methylene disalicylate and streptomycin sulfate tablets.

548.112d Soluble bacitracin methylene disalicylate and streptomycin sulfate oral powder.

548.114 Bacitracin zinc oral.

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Sec.

Subpart B—[Reserved]

Subpart C—Ophthalmic and Topical Dosage Forms

548.314 Bacitracin, bacitracin zinc ophthalmic and topical dosage forms.

548.314a Bacitracin, bacitracin zinc-neomycin sulfate-polymyxin B sulfate ophthalmic ointment.

548.314b Bacitracin zinc, polymyxin B sulfate, neomycin sulfate, hydrocortisone acetate, ophthalmic ointment.

AUTHORITY: Sec. 512, 82 Stat. 343-351 (21 U.S.C. 360b); 21 CFR 5.10, 5.83.

SOURCE: 40 FR 13933, Mar. 27, 1975, unless otherwise noted.

Subpart A—Oral Dosage Forms

§ 548.112 Bacitracin methylene disalicylate oral dosage forms.

§ 548.112a Bacitracin methylene disalicylate soluble powder.

(a) *Requirements for certification.*

(1) *Standards of identity, strength, quality, and purity.* The drug is soluble bacitracin methylene disalicylate with suitable and harmless diluents. It contains the equivalent of 50 grams of bacitracin activity per pound as defined in § 430.6(a)(2) of this chapter except that it contains the equivalent of 200 grams of bacitracin activity per pound as so defined if used as provided for in paragraph (c)(5)(ii)(c) of this section. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the labeled amount of bacitracin. Its loss on drying is not more than 8.5 percent. Its pH is not less than 8.0 and not more than 9.5. The soluble bacitracin methylene disalicylate used conforms to the standards prescribed by § 539.310b(a) of this chapter.

(2) *Labeling.* In addition to the requirements of § 510.55 of this chapter and paragraph (c) of this section, each package shall bear on the outside wrapper or container and the immediate container, the number of units of bacitracin per gram, the number of grams of bacitracin activity per pound, and the weight of the drug in the immediate container.

(3) *Requests for certification; samples.* In addition to complying with the

requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:
(a) The bacitracin methylene disalicylate used in making the batch for potency, loss on drying, and pH.

(b) The batch for potency, loss on drying, and pH.

(ii) Samples required:

(a) The soluble bacitracin methylene disalicylate used in making the batch: 5 packages, each containing approximately 5 grams.

(b) The batch: a minimum of 6 immediate containers, unless each such container is packaged to contain more than 30 grams, in which case the sample shall consist of 30 grams for each 5,000 containers in the batch, but in no case less than six 30-gram portions.

(b) Tests and methods of assay—(1) Potency. Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place an accurately weighed representative portion of the sample into a high-speed glass blender jar. Add 99 milliliters of 2 percent sodium bicarbonate solution (solution 14) and 1 milliliter of polysorbate 80. Blend 3 minutes. Allow the foam to subside. Remove an aliquot of the solution and dilute with 1 percent potassium phosphate buffer, pH 6.0, (solution 1) to the reference concentration of 1.0 unit of bacitracin per milliliter (estimated). At the reference concentration, the sample must have the same acidity as the standard, adding 0.01N HCl as needed.

(2) Loss on drying. Proceed as directed in § 436.200(b) of this chapter.

(3) pH. Proceed as directed in § 436.202 of this chapter, using a solution containing approximately 50 milligrams of sample per milliliter.

(c) Conditions of marketing—(1) Specifications. The drug conforms to the certification requirements of paragraph (a) of this section.

(2) Sponsor. See No. 046573 in § 510.600(c) of this chapter.

(3) Special considerations. Antibiotic activities authorized in paragraph (c)(5) of this section are expressed in terms of the weight of the appropriate antibiotic standard.

(4) Related tolerances. See § 556.70 of this chapter.

(5) Conditions of use. It is used in drinking water as follows:

(i) Growing turkeys—(a) Amount per gallon. 400 milligrams.

(1) Indications for use. Aid in control of transmissible enteritis complicated by organisms susceptible to bacitracin methylene disalicylate.

(2) Limitations. Prepare a fresh solution daily.

(b) [Reserved]

(ii) Broiler chickens—(a) Amount per gallon. 100 milligrams.

(1) Indications for use. Aid in prevention of necrotic enteritis caused by *Clostridium perfringens* susceptible to bacitracin methylene disalicylate.

(2) Limitations. Prepare a fresh solution daily.

(b) Amount per gallon. 200 to 400 milligrams.

(1) Indications for use. Aid in control of necrotic enteritis caused by *C. perfringens* susceptible to bacitracin methylene disalicylate.

(2) Limitations. Prepare a fresh solution daily.

(iii) Swine—(a) Amount per gallon. One gram.

(1) Indications for use. For treatment of swine dysentery associated with *Treponema hyodysenteriae*. Administer continuously for 7 days or until signs of dysentery disappear.

(2) Limitations. Prepare a fresh solution daily. Treatment not to exceed 14 days. If symptoms persist after 4 to 5 days consult a veterinarian. Not to be given to swine that weigh more than 250 pounds.

(b) [Reserved]

[40 FR 13933, Mar. 27, 1975, as amended at 44 FR 22054, Apr. 13, 1979; 45 FR 81039, Dec. 9, 1980; 47 FR 17986, Apr. 27, 1982; 47 FR 42102, Sept. 24, 1982; 50 FR 19923, May 13, 1985]

§ 548.112b Bacitracin methylene disalicylate and streptomycin sulfate tablets.

(a) Requirements for certification—

(1) Standards of identity, strength, quality, and purity. Bacitracin methylene disalicylate and streptomycin sulfate tablets are composed of bacitracin methylene disalicylate and streptomycin sulfate with carob flour and with or without one or more suitable and harmless diluents, binders, fillers, lu-

bricants or flavorings. Each tablet contains 150 units of bacitracin methylene disalicylate, streptomycin sulfate equivalent to 15 milligrams of streptomycin, and 875 milligrams of carob flour, or 1,000 units of bacitracin methylene disalicylate, streptomycin sulfate equivalent to 100 milligrams streptomycin, and 2.8 grams of carob flour. Its bacitracin methylene disalicylate content is satisfactory if it is 90 to 145 percent of the amount of bacitracin that it is represented to contain. Its streptomycin sulfate content is satisfactory if it is 90 to 135 percent of the amount of streptomycin that it is represented to contain. Its loss on drying is not more than 5 percent. Tablets not exceeding 15 millimeters in diameter shall disintegrate within 1 hour. The bacitracin methylene disalicylate used conforms to the standards prescribed by § 539.310a(a)(1) of this chapter. The streptomycin sulfate used conforms to the standards prescribed by § 539.170(a)(1) of this chapter.

(2) *Labeling.* It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) The results of tests and assays on:

- The bacitracin methylene disalicylate used in making the batch for potency, loss on drying, and pH.

- The streptomycin sulfate used in making the batch for potency, loss on drying, and pH.

- The batch for bacitracin content, streptomycin content, and loss on drying.

(ii) *Samples required:*

- The bacitracin methylene disalicylate used in making the batch, 5 packages, each containing approximately 5 grams.

- The streptomycin sulfate used in making the batch, 5 packages, each containing approximately 1 gram.

- The batch: a minimum of 36 tablets.

(b) *Tests and methods of assay—(1) Potency—(i) Bacitracin content.* Proceed as directed in § 436.105 of this chapter, preparing the sample for

assay as follows: Place a representative number of finely ground tablets in high-speed glass blender jar. Add sufficient dimethylformamide so that when the sample is diluted to its reference concentration, the concentration of dimethylformamide in the final solution is not more than 20 percent. Blend 3 to 5 minutes. Filter through filter paper immediately. Remove an aliquot of the filtrate at once and dilute with 1 percent potassium phosphate buffer, pH 6.0 (solution 1) to the reference concentration of 1 unit bacitracin per milliliter (estimated). Add sufficient dimethylformamide to the working solution of the standard so that the concentration of dimethylformamide is the same as that in the sample being tested. In lieu of the test organisms prescribed by § 436.105(a) of this chapter, use either the test organisms R or V described in § 436.103 of this chapter.

(ii) *Streptomycin content.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place a representative number of finely ground tablets in a high-speed glass blender jar. Add sufficient 0.1 percent potassium phosphate buffer, pH 6.0 (solution 3) to give a stock solution of convenient concentration. Add 1 milliliter of polysorbate 80 and blend 3 to 5 minutes. Allow to stand at room temperature for 1 hour. Blend again for 3 to 5 minutes. Pour contents of blender jar into a beaker, stir with a magnetic stirrer and while stirring, remove an aliquot and dilute with solution 3 to the reference concentration of 1.0 microgram of streptomycin per milliliter (estimated).

(2) *Loss on drying.* Proceed as directed in § 436.200(b) of this chapter.

(3) *Disintegration time.* Proceed as directed in § 436.212 of this chapter.

(c) *Conditions of marketing—Specifications.* The drug conforms to the requirements for certification in paragraph (a) of this section.

(2) *Sponsor.* No. 011716 of § 510.600(c) of this chapter.

(3) *Conditions of use—(i) Dosage—Amount.* One small tablet per pound of body weight, or one large tablet per 25 pounds of body weight, times daily.

(b) *Indications for use.* It is used for the treatment of dogs for bacterial enteritis caused by pathogens susceptible to bacitracin and streptomycin such as *Escherichia coli*, *Proteus* spp., *Staphylococcus* spp., and *Streptococcus* spp., and for the symptomatic treatment of associated diarrhea.

(c) *Limitations.* If no improvement is noted in 2 to 3 days, diagnosis should be reevaluated. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[42 FR 38566, July 29, 1977; 42 FR 47192, Sept. 20, 1977; 44 FR 22055, Apr. 13, 1979, as amended at 50 FR 19923, May 13, 1985]

§ 548.112j Soluble bacitracin methylene disalicylate and streptomycin sulfate oral powder.

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality, and purity.* Soluble bacitracin methylene disalicylate and streptomycin sulfate oral powder is composed of soluble bacitracin methylene disalicylate and streptomycin sulfate with carob flour and with or without one or more suitable and harmless diluents, colorings, and flavorings. Each gram contains 200 units of soluble bacitracin methylene disalicylate, streptomycin sulfate equivalent to 20 milligrams of streptomycin, and 850 milligrams of carob flour. Its soluble bacitracin methylene disalicylate content is satisfactory if it is 90 to 165 percent of the amount of bacitracin that it is represented to contain. Its streptomycin sulfate content is satisfactory if it is 90 to 125 percent of the amount of streptomycin that it is represented to contain. Its loss on drying is not more than 7.5 percent. The soluble bacitracin methylene disalicylate used conforms to the standards prescribed by § 548.112a of this chapter for soluble bacitracin methylene disalicylate without diluents. The streptomycin sulfate used conforms to the standards prescribed by § 539.170(a)(1) of this chapter.

(2) *Labeling.* It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the

requirements of § 514.50 of this chapter, each such request shall contain:

(i) The results of tests and assays on:

(a) The soluble bacitracin methylene disalicylate used in making the batch for potency, loss on drying, and pH.

(b) The streptomycin sulfate used in making the batch for potency, loss on drying, and pH.

(c) The batch for bacitracin content, streptomycin content, and loss on drying.

(ii) *Samples required:*

(a) The soluble bacitracin methylene disalicylate used in making the batch, 5 packages, each containing approximately 5 grams.

(b) The streptomycin sulfate used in making the batch, 5 packages, each containing approximately 1 gram.

(c) The batch: a minimum of 6 immediate containers, unless each such container is packaged to contain more than 30 grams, in which case the sample shall consist of 30 grams for each 5,000 containers in the batch, but in no case less than six 30-gram portions.

(b) *Tests and methods of assay—*(1) *Potency—*(i) *Bacitracin content.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place an accurately weighed sample of approximately 5 grams into a high-speed glass blender jar. Add sufficient dimethylformamide so that when the sample is diluted to its reference concentration, the concentration of dimethylformamide in the final solution is not more than 20 percent. Blend 3 to 5 minutes. Filter through filter paper immediately. Remove an aliquot of the filtrate at once and dilute with 1 percent potassium phosphate buffer, pH 6.0 (solution 1) to the reference concentration of 1 unit of bacitracin per milliliter (estimated). Add sufficient dimethylformamide to the working solution of the standard so that the concentration of dimethylformamide is the same as that in the sample being tested. In lieu of the test organisms prescribed in § 436.105(a), use either of the test organisms R or V described in § 436.103(a) of this chapter.

(ii) *Streptomycin content.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as fol-

lows: Dissolve an accurately weighed sample in sufficient 0.1 M potassium phosphate buffer, pH 8.0 (solution 3) to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with solution 3 to the reference concentration of 1.0 microgram of streptomycin per milliliter (estimated).

(2) *Loss on drying.* Using a 1.0-gram sample proceed as directed in § 436.200 (b) of this chapter.

(c) *Conditions of marketing.*—(1) *Specifications.* The drug conforms to the requirements for certification in paragraph (a) of this section.

(2) *Sponsor.* No. 011716 in § 510.600(c) of this chapter.

(3) *Conditions of use.*—(i) *Dogs.*—(a) *Amount.* One level teaspoonful per 10 pounds of body weight three times daily, in a small quantity of liquid or feed.

(b) *Indications for use.* It is used for the treatment of dogs for bacterial enteritis caused by pathogens susceptible to bacitracin and streptomycin, such as *Escherichia coli*, *Proteus* spp., *Staphylococcus* spp., and *Streptococcus* spp., and for the symptomatic treatment of associated diarrhea.

(c) *Limitations.* If no improvement is noted in 2 to 3 days, diagnosis should be reevaluated. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[42 FR 38565, July 29, 1977; 42 FR 47192, Sept. 20, 1977, as amended at 43 FR 48997, Oct. 20, 1978; 43 FR 59059, Dec. 19, 1978; 50 FR 19923, May 13, 1985]

§ 548.114 Bacitracin zinc soluble powder.

(a) *Requirements for certification.*—

(1) *Standards of identity, strength, quality, and purity.* The drug is a mixture of unrefined bacitracin zinc and zinc proteinates with or without one or more suitable and harmless diluents, flavorings, and colorings. It contains the equivalent of not less than 5 grams of bacitracin, as defined in § 430.6(a)(2) of this chapter, per pound. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the labeled amount of bacitracin. Its loss on drying is not more than 5 percent. The unrefined bacitracin zinc used has a potency of not less than 2 units per

milligram, its zinc content is not more than 2 grams for each gram of bacitracin, and its loss on drying is not more than 6 percent.

(2) *Labeling.* It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The unrefined bacitracin zinc used in making the batch for potency, loss on drying, and zinc content.

(b) The batch for potency and loss on drying.

(ii) Samples required:

(a) The unrefined bacitracin zinc used in making the batch: 3 packages, each consisting of a composite of 6 portions of approximately 500 milligrams, each taken at random from different locations in the batch.

(b) The batch: a minimum of 6 immediate containers, unless each such container is packaged to contain more than 30 grams, in which case the sample shall consist of 30 grams for each 5,000 containers, but in no case less than six 30-gram portions.

(b) *Tests and methods of assay.*—(1)

Unrefined bacitracin zinc used in making the batch.—(i) *Potency.* Proceed as directed for bacitracin zinc in § 436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in sufficient 0.01N hydrochloric acid to give a bacitracin concentration of 100 units per milliliter (estimated). Further dilute an aliquot with 1 percent potassium phosphate buffer, pH 6.8, (solution 1) to the reference concentration of 1.0 unit of bacitracin per milliliter (estimated). At the reference concentration, the sample and standard must have the same acidity, adding 0.01N HCl as needed.

(ii) *Loss in drying.* Proceed as directed in § 436.200(b) of this chapter.

(iii) *Zinc content.* Proceed as directed in § 436.312 of this chapter.

(2) *Bacitracin zinc soluble powder.*

(i) *Potency.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in

Subpart B—[Reserved]

Subpart C—Ophthalmic and Topical Dosage Forms

§ 548.314 Bacitracin, bacitracin zinc ophthalmic and topical dosage forms.

[44 FR 22056, Apr. 13, 1979]

§ 548.314a Bacitracin, bacitracin zinc-neomycin sulfate-polymyxin B sulfate ophthalmic ointment.

(a) *Requirements for certification—*
(1) *Standards of identity, strength, quality, and purity.* The drug contains bacitracin or bacitracin zinc, neomycin sulfate, and polymyxin B sulfate in a suitable and harmless ointment base. Each gram contains:

(i) 500 units of bacitracin, 3.5 milligrams of neomycin, and 10,000 units of polymyxin B.

(ii) 400 units of bacitracin zinc, 3.5 milligrams of neomycin, and 10,000 units of polymyxin B.

Its bacitracin or bacitracin zinc content is satisfactory if it is not less than 90 percent and not more than 140 percent of the labeled amount of bacitracin. Its neomycin sulfate content is satisfactory if it is not less than 90 percent and not more than 140 percent of the labeled amount of neomycin. Its polymyxin B sulfate content is satisfactory if it is not less than 90 percent and not more than 140 percent of the labeled amount of polymyxin B. It is sterile. Its moisture content is not more than 0.5 percent. It passes the test for metal particles. The bacitracin used conforms to the standards prescribed by § 448.10a(a)(1) of this chapter. The bacitracin zinc used conforms to the standards prescribed by § 448.13a(a)(1) of this chapter. The neomycin sulfate used conforms to the standards prescribed by § 444.42a(a)(1), except for pyrogens. The polymyxin B sulfate used conforms to the standards prescribed by § 448.30a(a)(1), except for pyrogens and residue on ignition.

(2) *Labeling.* It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the

sufficient 0.01N hydrochloric acid to give a bacitracin concentration of 100 units per milliliter (estimated). Further dilute an aliquot with solution 1 to the reference concentration of 1.0 unit of bacitracin per milliliter (estimated). At the reference concentration, the sample and standard must have the same acidity, adding 0.01N HCl as needed.

(ii) *Loss in drying.* Proceed as directed in § 436.200(b) of this chapter.

(c) *Conditions of marketing—*(1) *Specifications.* The drug contains 50 grams of bacitracin activity per pound, and conforms to the certification requirements of paragraph (a) of this section.

(2) *Sponsor.* See No. 011716 in § 510.600(c) of this chapter.

(3) *Special considerations.* Quantities of bacitracin zinc expressed in paragraph (c)(5) of this section refer to the weight of an appropriate antibiotic standard.

(4) *Related tolerances.* See § 556.70 of this chapter.

(5) *Conditions of use.* It is used in drinking water as follows:

(i) *Broiler chickens—*(a) *Amount per gallon.* 100 milligrams.

(1) *Indications for use.* Prevention of necrotic enteritis caused by *Clostridium perfringens* susceptible to bacitracin zinc.

(2) *Limitations.* Prepare a fresh solution daily.

(b) *Amount per gallon.* 200 to 400 milligrams.

(1) *Indications for use.* Control of necrotic enteritis caused by *Clostridium perfringens* susceptible to bacitracin zinc.

(2) *Limitations.* Prepare a fresh solution daily.

(ii) *Growing quail—*(a) *Amount per gallon.* 500 milligrams for 5 days followed by 165 milligrams for 10 days.

(b) *Indications for use.* Control of ulcerative enteritis caused by *Clostridium* spp. susceptible to bacitracin zinc.

(c) *Limitations.* Prepare a fresh solution daily.

[40 FR 13033, Mar. 27, 1975, as amended at 42 FR 27240, May 27, 1977; 44 FR 22055, Apr. 13, 1979; 47 FR 24694, June 8, 1982; 53 FR 20843, June 7, 1988]

requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The bacitracin or bacitracin zinc used in making the batch for potency, loss on drying, pH, zinc content if applicable, and identity.

(b) The neomycin sulfate used in making the batch for potency, loss on drying, pH, and identity.

(c) The polymyxin B sulfate used in making the batch for potency, loss on drying, pH, and identity.

(d) The batch for bacitracin or bacitracin zinc content, neomycin content, polymyxin B content, sterility, moisture, and metal particles.

(ii) Samples required:

(a) The bacitracin or bacitracin zinc used in making the batch: 10 packages, each containing approximately 1.0 gram.

(b) The neomycin sulfate used in making the batch: 10 packages, each containing approximately 1.0 gram.

(c) The polymyxin B sulfate used in making the batch: 10 packages, each containing approximately 1.0 gram.

(d) The batch:

(1) For all tests except sterility: A minimum of 17 immediate containers.

(2) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1)

Potency—(i)(a) *Bacitracin content*. Proceed as directed for bacitracin zinc in § 436.105 of this chapter, preparing the sample for assay as follows: Place an accurately weighed representative portion of the sample into a separatory funnel containing approximately 50 milliliters of peroxide-free ether. Shake the sample and ether until homogeneous. Add 20 to 25 milliliters of 1.0 percent potassium phosphate buffer, pH 6.0 (solution 1), and shake well. Allow the layers to separate. Remove the buffer layer and repeat the extraction procedure with each of three more 20- to 25-milliliter quantities of solution 1. Combine the buffer extractives in a suitable volumetric flask and dilute to volume with solution 1. Remove an aliquot, add sufficient hydrochloric acid so that the amount of acid in the final solution will be the same as in the reference

concentration of the working standard and further dilute with solution 1 to the reference concentration of 1.0 unit of bacitracin per milliliter (estimated).

(b) *Bacitracin zinc content*. Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place an accurately weighed representative portion of the sample into a separatory funnel containing approximately 50 milliliters of peroxide-free ether. Shake the sample and ether until they are homogeneous. Add 20 to 25 milliliters of 0.01N hydrochloric acid and shake well. Allow the layers to separate. Remove the acid layer and repeat the extraction procedure with each of three more 20- to 25-milliliter quantities of 0.01N hydrochloric acid. Combine the acid extractives in a suitable volumetric flask and dilute to volume with 0.01N hydrochloric acid. (If the bacitracin content is less than 100 units per milliliter in 0.01N hydrochloric acid, add sufficient additional hydrochloric acid to each standard response line concentration so that each standard solution contains the same amount of acid as the 1.0 unit per milliliter sample solution.) Remove an aliquot and further dilute with 1 percent potassium phosphate buffer, pH 6.0 (solution 1) to the reference concentration of 1.0 unit of bacitracin per milliliter (estimated).

(ii) *Neomycin content*. Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place an accurately weighed representative portion of the sample into a separatory funnel containing approximately 50 milliliters of peroxide-free ether. Shake the sample and ether until homogeneous. Add 20 to 25 milliliters of 0.1M potassium phosphate buffer, pH 8.0, (solution 3) and shake well. Allow the layers to separate. Remove the buffer layer and repeat the extraction procedure with each of three more 20- to 25-milliliter quantities of solution 3. Combine the buffer extractives in a suitable volumetric flask and dilute to volume with solution 3. Remove an aliquot and further dilute with solution 3 to the reference concentration of 1.0 microgram of neomycin per milliliter (estimated).

(iii) *Polymyxin B content*. Proceed as directed in § 436.105 of this chapter.

except add to each polymyxin B standard response line concentration a quantity of neomycin to yield the same concentration of neomycin as that present when the sample is diluted to contain 10 units of polymyxin B per milliliter. Prepare the sample for assay as follows: Place an accurately weighed representative portion of the sample into a separatory funnel containing approximately 50 milliliters of peroxide-free ether. Shake the sample and ether until homogeneous. Add 20 to 25 milliliters of 10 percent potassium phosphate buffer, pH 6.0, (solution 6) and shake well. Allow the layers to separate. Remove the buffer layer and repeat the extraction procedure with each of three more 20- to 25-milliliter quantities of solution 6. Combine the buffer extractives in a suitable volumetric flask and dilute with solution 6 to the reference concentration of 10 units of polymyxin B per milliliter (estimated).

(2) *Sterility*. Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(3) of that section.

(3) *Moisture*. Proceed as directed in § 436.201 of this chapter.

(4) *Metal particles*. Proceed as directed in § 436.206 of this chapter.

(c) *Conditions of marketing*—(1) *Specifications*. The drug conforms to the certification requirements of paragraph (a) of this section.

(2) *Sponsor*. To firms identified by drug listing numbers in § 510.600(c) of this chapter, approvals as follows:

(i) To 000009; for a drug containing in each gram 500 units of bacitracin, 3.5 milligrams of neomycin, and 10,000 units of polymyxin B.

(ii) To 017220 and 025463; for a drug containing in each gram, 400 units or bacitracin zinc, 3.5 milligrams of neomycin, and 10,000 units of polymyxin B sulfate.

(3) *Conditions of use*. (i) The drug is used in the treatment of superficial bacterial infections of the eyelid and conjunctiva of dogs and cats when due to organisms susceptible to the antibiotics contained in the ointment.

(ii) Apply a thin film over the cornea 3 or 4 times daily. Laboratory tests should be conducted including in vitro culturing and susceptibility tests on

samples collected from animals prior to treatment with the drug.

(iii) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[44 FR 22056, Apr. 13, 1979, as amended at 46 FR 13215, Feb. 20, 1981; 46 FR 48642, Oct. 2, 1981; 50 FR 19923, May 13, 1985; 51 FR 19546, May 30, 1986]

§ 548.314b Bacitracin: zinc-polymyxin B sulfate-neomycin sulfate-hydrocortisone, hydrocortisone acetate ophthalmic ointment.

(a) *Requirements for certification*. The requirements for certification for the drug are described in § 548.314a(a), except that each gram of drug contains: (1) 400 units of bacitracin zinc, 10,000 units of polymyxin B sulfate, 5 milligrams of neomycin sulfate (equivalent to 3.5 milligrams of neomycin base), and 10 milligrams of hydrocortisone; or (2) 400 units of bacitracin zinc, 10,000 units of polymyxin B sulfate, 5 milligrams of neomycin sulfate (equivalent to 3.5 milligrams of neomycin base), and 10 milligrams of hydrocortisone acetate.

(b) *Tests and methods of assay*. The tests and methods of assay are described in § 548.314a(b).

(c) *Conditions of marketing*—(1) *Specifications*. The drug conforms to the certification requirements of paragraph (a) of this section.

(2) *Sponsor*. See 017220 for product described in paragraph (a)(1), see 025463 for product described in paragraph (a)(2) of this section.

(3) *Conditions of use*. (i) The drug is administered to dogs and cats for treating acute or chronic conjunctivitis caused by organisms susceptible to the antibiotics contained in this ointment.

(ii) Apply a thin film over the cornea three or four times daily.

(iii) All topical ophthalmic preparations containing corticosteroids with or without an antimicrobial agent are contraindicated in the initial treatment of corneal ulcers. They should not be used until the infection is under control and corneal regeneration is well underway.

§ 555.110a

(iv) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[40 FR 13933, Mar. 27, 1975, as amended at 44 FR 22057, Apr. 13, 1979; 45 FR 27925, Apr. 25, 1980; 46 FR 48642, Oct. 2, 1981; 51 FR 19546, May 30, 1986]

**PART 555—CHLORAMPHENICOL
DRUGS FOR ANIMAL USE**

Subpart A—Oral Dosage Forms

Sec.

555.110 Chloramphenicol oral dosage forms.

555.110a Chloramphenicol tablets.

555.110b Chloramphenicol capsules.

555.111 Chloramphenicol palmitate oral suspension.

Subpart B—Implantation or Injectable Dosage Forms

555.210 Chloramphenicol injection.

Subpart C—Ophthalmic and Topical Dosage Forms

555.310 Chloramphenicol ophthalmic and topical dosage forms.

555.310a Chloramphenicol ophthalmic.

555.310b Chloramphenicol topical.

555.310c Chloramphenicol ophthalmic ointment.

555.310d Chloramphenicol ophthalmic solution.

555.310e Chloramphenicol-prednisolone-tetracaine-squalane topical suspension.

555.310f Chloramphenicol-prednisolone ophthalmic ointment.

Subpart D—Otic Dosage Forms

555.410 Chloramphenicol otic.

AUTHORITY: Sec. 512(i) and (n), 82 Stat. 347, 350-351 (21 U.S.C. 360b (i) and (n)); 21 CFR 5.10 and 5.83.

SOURCE: 40 FR 13938, Mar. 27, 1975, unless otherwise noted.

Subpart A—Oral Dosage Forms

§ 555.110 Chloramphenicol oral dosage forms.

§ 555.110a Chloramphenicol tablets.

(a) *Requirements for certification—*
(1) *Standards of identity, strength, quality, and purity.* Chloramphenicol tablets are composed of chloramphenicol with or without one or more suitable diluents, lubricants, binders, color-

ings and coating substances. Each tablet contains 100, 250, or 500 milligrams, 1 or 2.5 grams of chloramphenicol. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of chloramphenicol that it is represented to contain. Tablets shall disintegrate within 1 hour. The chloramphenicol used conforms to the standards prescribed by § 455.10(a)(1) of this chapter.

(2) *Labeling.* It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The chloramphenicol used in making the batch for potency, pH, specific rotation, melting range, absorptivity, and crystallinity.

(b) The batch for potency and disintegration time.

(ii) Samples required.

(a) The chloramphenicol used in making the batch: 10 packages each containing approximately 300 milligrams.

(b) The batch: A minimum of 30 tablets.

(b) *Tests and methods of assay—*(1) *Potency.* Use either of the following methods; however, the results obtained from the microbiological turbidimetric assay shall be conclusive.

(i) *Microbiological turbidimetric assay.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Place a representative number of tablets into a high-speed glass blender jar containing 100 milliliters of 95 percent ethyl alcohol. Blend for 2 minutes. Add 400 milliliters of distilled water and blend again for 2 minutes. Remove an aliquot and further dilute with distilled water to the reference concentration of 2.5 micrograms of chloramphenicol per milliliter (estimated).

(ii) *Spectrophotometric assay—*(a) *Preparation of working standard solution.* Dissolve approximately 50 milligrams of the working standard in 100 milliliters of distilled water. Warm if necessary to hasten dissolution. Trans-

fer 10 milliliters into a 250-milliliter volumetric flask and fill to volume with distilled water.

(b) *Procedure.* Weigh accurately a counted number of not less than 10 tablets and determine the average weight per tablet. Reduce 10 tablets to a fine powder in a mortar and transfer an amount of powder containing 500 milligrams (estimated) of chloramphenicol to a 1,000-milliliter glass-stoppered volumetric flask. Add 50 milliliters of redistilled methanol to the flask and shake for at least 1

minute. Fill to volume with distilled water and mix thoroughly. Transfer exactly 10 milliliters of this solution into a 250-milliliter glass-stoppered volumetric flask. Fill to volume with distilled water and mix thoroughly. Determine the absorbance of this solution on a suitable spectrophotometer in a 1-centimeter quartz cell at 278 nanometers against a blank of distilled water. Calculate the potency of the sample as follows:

Milligrams of chloramphenicol per tablet=

Absorbance of sample solution	x	Concentration of working standard solution (mg/ml)	x	Potency of working standard (mcg/mg)	x	25,000	x	Average tablet weight (mg/tab)
		Absorbance of working standard solution	x	Weight of sample (mg)	x	1000		

(2) *Disintegration time.* Proceed as directed in § 436.212 of this chapter.

(c) *Conditions of marketing—(1)(i) Specifications.* Chloramphenicol tablets conform to the certification requirements of paragraph (a) of this section.

(ii) *Sponsor.* In § 510.600(c) of this chapter, No. 000010 for 100-, 250-, and 500-milligram and 1-gram tablets; No. 000856 for 100-, 250-, and 500-milligram tablets; No. 017030 for 100-milligram tablets; No. 054273 for 100-, 250-, and 500-milligram and 1- and 2.5-gram tablets; No. 000069 for 250-milligram tablets.

(iii) *Conditions of use.* (a) The drug is administered to dogs for oral treatment of bacterial pulmonary infections, bacterial infections of the urinary tract, bacterial enteritis, and bacterial infections associated with canine distemper caused by susceptible organisms.

(b) The drug is administered at 25 milligrams per pound of body weight every 6 hours.

(c) Laboratory tests should be conducted, including in vitro culturing and susceptibility tests on samples collected prior to treatment. If no response to chloramphenicol therapy is obtained in 3 to 5 days, discontinue its use and review diagnosis.

(d) The label bears a statement that the product is not to be used in animals which are raised for food production.

(e) Chloramphenicol products must not be used in meat-, egg-, or milk-producing animals. The length of time that residues persist in milk or tissues has not been determined. Because of potential antagonism, chloramphenicol should not be administered simultaneously with penicillin or streptomycin.

(f) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(2)(i) *Specifications.* Chloramphenicol tablets, contain 50, 100, 250, or 500 milligrams, or 1 gram of chloramphenicol and conform to the certification requirements of paragraph (a) of this section.

(ii) *Sponsor.* See No. 053617 in § 510.600(c) of this chapter.

(iii) *Conditions of use.* (a) The drug is administered to dogs for oral treatment of bacterial gastroenteritis associated with bacterial diarrhea, bacterial pulmonary infections, and bacterial infections of the urinary tract caused by susceptible organisms.

(b) The drug is administered at 25 milligrams per pound of body weight every 6 hours.

(c) Laboratory tests should be conducted, including in vitro culturing and susceptibility tests on samples collected prior to treatment. If no response to chloramphenicol therapy is obtained in 3 to 5 days, discontinue its use and review diagnosis.

(d) The label bears a statement that the product is not to be used in animals that are raised for food production.

(e) Chloramphenicol products should not be administered in conjunction with or 2 hours prior to the induction of general anesthesia with pentobarbital because of prolonged recovery. Chloramphenicol should not be administered to dogs maintained for breeding purposes. Because of potential antagonism, chloramphenicol should not be administered simultaneously with penicillin or streptomycin.

(f) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(Secs. 507, 512(n), 701 (f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371 (f) and (g)))

[40 FR 13938, Mar. 27, 1975, as amended at 40 FR 26273, June 23, 1975; 41 FR 55175, Dec. 17, 1976; 42 FR 14096, Mar. 15, 1977; 48 FR 3961, Jan. 28, 1983; 48 FR 6331, Feb. 11, 1983; 48 FR 10302, Mar. 11, 1983; 48 FR 33865, July 26, 1983; 49 FR 48184, Dec. 11, 1984; 50 FR 19923, May 13, 1985; 50 FR 49373, Dec. 2, 1985; 50 FR 49924, Dec. 6, 1985; 53 FR 23390, June 22, 1988; 53 FR 40728, Oct. 18, 1988]

§ 555.110b Chloramphenicol capsules.

(a) Requirements for certification—

(1) *Standards of identity, strength, quality, and purity.* Chloramphenicol capsules are composed of chloramphenicol with or without one or more suitable diluents and lubricants. Each capsule contains 50, 100, 250, or 500 milligrams of chloramphenicol. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of chloramphenicol that it is represented to contain. The chloramphenicol used conforms to the standards prescribed by § 455.10(a)(1) of this chapter.

(2) *Labeling.* In addition to the labeling requirements of paragraph (c) of

this section and § 510.55 of this chapter, its label and labeling shall bear the statement, "Warning: Not for use in animals which are raised for food production".

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The chloramphenicol used in making the batch for potency, pH, specific rotation, melting range, absorptivity, and crystallinity.

(b) The batch for potency.

(ii) Samples required:

(a) The chloramphenicol used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch: A minimum of 30 capsules.

(b) *Tests and methods of assay: potency.* Proceed as directed in § 455.110(b) of this chapter.

(c) *Conditions of marketing—(1) Specifications.* Chloramphenicol capsules contain 50, 100, 250, and 500 milligrams of chloramphenicol and conform to the certification requirements of paragraph (a) of this section.

(2) *Sponsor.* (i) For chloramphenicol capsules containing 50, 100, 250 and 500 milligrams chloramphenicol see Nos. 000069, 000172, 027454, and 052492 in § 510.600(c) of this chapter.

(ii) For chloramphenicol capsules containing 100 and 250 milligrams of chloramphenicol see No. 000022 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) The drug is administered to dogs for oral treatment of bacterial pulmonary infections, bacterial infections of the urinary tract, bacterial enteritis, and bacterial infections associated with canine distemper caused by susceptible organisms.

(ii) The drug is administered at 25 milligrams per pound of body weight every 6 hours.

(iii) Laboratory tests should be conducted including in vitro culturing and susceptibility tests on samples collected prior to treatment.

(iv) This product must not be used in meat, egg, or milk producing animals. The length of time that residues per-

sist in milk or tissues has not been determined.

(v) For use by or on the order of a licensed veterinarian.

(40 FR 13938, Mar. 27, 1975, as amended at 49 FR 30615, July 5, 1983; 49 FR 19641, May 9, 1984; 50 FR 19923, May 13, 1985; 51 FR 11441, Apr. 3, 1986)

§ 555.111 Chloramphenicol palmitate oral suspension.

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality, and purity.* Chloramphenicol palmitate oral suspension is chloramphenicol palmitate and one or more suitable and harmless buffer substances, suspending agents, preservatives, colorings, and flavorings suspended in a suitable and harmless vehicle. Each milliliter contains chloramphenicol palmitate equivalent to 30.0 milligrams of chloramphenicol. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the amount of chloramphenicol that it is represented to contain. Its pH is not less than 4.5 or more than 7.0. Its content of polymorph A crystals does not exceed 10 percent. The chloramphenicol palmitate used conforms to the standards prescribed by § 455.11(a)(1) of this chapter.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 510.55 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The chloramphenicol palmitate used in making the batch for chloramphenicol content, melting range, specific rotation, and crystallinity.

(b) The batch for chloramphenicol content, pH, and content of polymorph A crystals.

(ii) Samples required:

(a) The chloramphenicol palmitate used in making the batch: 10 packages each containing approximately 500 milligrams.

(b) The batch: A minimum of six immediate containers.

(c) *Tests and methods of assay—*(1) *Chloramphenicol content (high-pressure liquid chromatography).* Proceed

as directed in § 436.335 of this chapter, except prepare the sample solution and calculate the chloramphenicol content as follows:

(i) *Preparation of sample solution.* Transfer a portion of the sample equivalent to 150 milligrams of chloramphenicol into a 200-milliliter volumetric flask. Add 100 milliliters of methanol and 4 milliliters of glacial acetic acid. Shake and dilute to volume with methanol. Filter the solution through a glass fiber filter or equivalent that is capable of removing particulate contamination to 1 micron in diameter.

(ii) *Calculations.* Calculate the chloramphenicol content as follows:

$$\frac{\text{Milligrams of chloramphenicol per milliliter}}{= \frac{(A)(W)(f)(4)}{(B)(1,000)(V)}}$$

where:

A=Area of the chloramphenicol palmitate sample peak (at a retention time equal to that observed for the standard);

B=Area of the working standard peak;

W=Weight of standard in milligrams;

f=Micrograms of chloramphenicol activity per milligram of chloramphenicol palmitate working standard; and

V=Volume of sample in milliliters.

(2) *pH.* Proceed as directed in § 436.202 of this chapter, using the undiluted sample.

(3) *Content of polymorph A crystal—*

(i) *Preparation of standards—*(a) *Standard containing 20 percent of polymorph A.* Prepare a thoroughly mixed, dry powder composed by weight of 1 part of polymorph A crystals of chloramphenicol palmitate and 4 parts of nonpolymorph A crystals of chloramphenicol palmitate.

(b) *Standard containing 10 percent of polymorph A.* Prepare a thoroughly mixed, dry powder composed by weight of 1 part of polymorph A crystals of chloramphenicol palmitate and 9 parts of nonpolymorph A crystals of chloramphenicol palmitate.

(ii) *Preparation of sample.* Place 20 milliliters of thoroughly mixed oral suspension into a 50-milliliter centrifuge tube. Add 20 milliliters of water and mix. Centrifuge for 10 to 15 minutes at a speed not less than 18,000 revolutions per minute. Decant the su-

pernatant liquid. Wash the residue as follows: Add 2 milliliters of water to the residue, mix to make paste, add 18 milliliters of water, and mix thoroughly. Centrifuge, decant the supernatant liquid, and wash the residue two more times. Remove the washed residue from the centrifuge tube and dry it at least 14 hours in a vacuum desiccator at room temperature.

(iii) *Procedure.* Weight 150 to 200 milligrams of liquid petrolatum into an agate mortar and add about 100 milligrams of standard or sample. Mix with a small spatula, and then mull thoroughly with a pestle until a uniform consistency is obtained. Adjust a suitable infrared spectrophotometer so that 100 percent transmittance is recorded over the range of 11.0 to 13.0 microns. Use two rock-salt plates as an absorption cell. Place a small drop of the mull in the center of one of the plates. Gently put the other plate on the mull and slowly squeeze the plates together to spread the mull uniformly. Clamp the two plates firmly together in a metal cell holder. Examine the assembled cell by holding it up to the light. It should appear smooth and free of any air bubbles, and when placed in the instrument it should give a percent transmittance of 20 to 30 percent at 12.3 microns. Place the cell in the infrared spectrophotometer and record the absorption spectrum from 11.0 to 13.0 microns.

(iv) *Treatment of spectra—(a) Standard containing 20 percent of polymorph A.* Determine by inspection of the recorded spectrum the exact wavelengths of minimum absorption at approximately 11.3 and 12.65 microns; also, determine by inspection the exact wavelengths of maximum absorption at approximately 11.65 and 11.86 microns. In paragraph (b)(3)(iv)(b) of this section, references to these four nominal wavelengths are the exact wavelengths observed on the particular instrument being used.

(b) *Standard containing 10 percent of polymorph A.* Draw a straight baseline between the minima occurring at 11.3 and 12.65 microns. Draw straight lines at 11.65 and 11.86 microns intersecting both the recorded spectrum and the baseline. Obtain the corrected absorbances at 11.65 and 11.86 microns

and calculate the absorbance ratio as follows:

$$\text{Absorbance ratio} = \frac{{}^{*}11.65 - {}^{*}11.85}{{}^{*}11.86 - {}^{*}11.85}$$

where:

^{*}11.65 = Absorbance value of recorded spectrum at 11.65 microns;

^{*}11.65 = Absorbance value at point of intersection of the 11.65-micron line with the baseline;

^{*}11.86 = Absorbance value of recorded spectrum at 11.86 microns;

^{*}11.86 = Absorbance value at point of intersection of the 11.86-micron line with the baseline.

(c) *Sample.* Proceed as described in paragraph (b)(3)(iv)(b) of this section.

(v) *Results and evaluation.* The absorbance ratio of the sample must be greater than the absorbance ratio of the standard containing 10 percent of polymorph A.

(c) *Conditions of marketing—(1) Specifications.* The product complies with the requirements of paragraph (a) of this section.

(2) *Sponsor.* No. 000856 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) It is used in dogs for the treatment of bacterial pulmonary infections, infections of the urinary tract, enteritis, and infections associated with canine distemper that are caused by organisms susceptible to chloramphenicol.

(ii) It is administered orally at a dosage of 25 milligrams per pound of body weight every 6 hours. If no response is obtained in 3 to 5 days, discontinue use and reevaluate diagnosis.

(iii) Not for use in animals that are raised for food production. Must not be used in meat, egg, or milk-producing animals. The length of time that residues persist in milk or tissues has not been determined.

(iv) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(Secs. 507, 512(n), 701 (f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371 (f) and (g)))

[41 FR 40972, Nov. 12, 1976, as amended at 49 FR 6094, Feb. 17, 1984; 50 FR 19923, May 13, 1985; 53 FR 23390, June 22, 1988]

Subpart B—Implantation or Injectable Dosage Forms

§ 555.210 Chloramphenicol injection.

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality, and purity.* Chloramphenicol injection is a solution containing chloramphenicol and one or more suitable and harmless buffers and preservatives in an organic solvent vehicle. Each milliliter contains 100 milligrams of chloramphenicol. The chloramphenicol content is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of chloramphenicol that it is represented to contain. It is sterile. It is nonpyrogenic. Its pH is not less than 6.5 and not more than 8.5. The chloramphenicol used conforms to the standards prescribed by § 455.10(a)(1) of this chapter.

(2) *Packaging.* It shall be packaged in accordance with the requirements of § 510.45 of this chapter.

(3) *Labeling.* It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 510.55 of this chapter.

(4) *Requests for certification; samples.* In addition to the requirements of § 514.50 of this chapter, each such request shall contain:

(i) *Results of tests and assays on:*

(a) The chloramphenicol used in making the batch for potency, pH, specific rotation, melting point, absorptivity, and crystallinity.

(b) The batch for potency, sterility, pyrogens, and pH.

(ii) *Samples required:*

(a) The chloramphenicol used in making the batch: 10 packages each containing approximately 300 milligrams.

(b) *The batch:*

(1) For all tests except sterility: A minimum of 8 immediate containers.

(2) For sterility testing: 20 immediate containers collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assays—(1) Potency.* Proceed as directed in

§ 436.106 of this chapter, preparing the sample for assay as follows: Dilute an accurately measured representative portion of the sample with distilled water to obtain a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with distilled water to the reference concentration of 2.5 micrograms of chloramphenicol per milliliter (estimated).

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section, except transfer 1 milliliter from each container directly to the dry filter, thus eliminating the preliminary solubilization step.

(3) *Pyrogens.* Proceed as directed in § 436.32(a) of this chapter.

(4)–(5) [Reserved]

(6) *pH.* Proceed as directed in § 436.202 of this chapter, diluting the sample with an equal volume of distilled water.

(c) *Conditions of marketing—(1) Specifications.* The product complies with the requirements of paragraph (a) of this section.

(2) *Sponsor.* See Nos. 000069, 010271, and 053617 in § 510.600(c) of this chapter.

(3) *Conditions of use—(i)* It is used in dogs for the treatment of infections of the respiratory tract, the urinary tract, and enteritis and tonsillitis caused by organisms susceptible to chloramphenicol.

(ii) It is administered intramuscularly or intravenously at a dosage level of 5 to 15 milligrams per pound of body weight every 6 hours. In severe infections, 4 to 6 hour treatment intervals may be desirable the first day of treatment. If no response to treatment is obtained in 3 to 5 days, use should be discontinued and the diagnosis reviewed.

(iii) The label bears a statement that the product is not to be used in animals which are raised for food production.

(iv) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(Secs. 507, 512(n), 701 (f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371 (f) and (g)))

§ 555.310a

[40 FR 13938, Mar. 27, 1975, as amended at 41 FR 30590, July 26, 1976; 41 FR 55175, Dec. 17, 1976; 45 FR 64568, Sept. 30, 1980; 48 FR 3961, Jan. 28, 1983; 48 FR 30615, July 5, 1983; 50 FR 19923, May 13, 1985; 50 FR 49373, Dec. 2, 1985]

Subpart C—Ophthalmic and Topical Dosage Forms

§ 555.310 Chloramphenicol ophthalmic and topical dosage forms.

§ 555.310a Chloramphenicol ophthalmic.

(a) *Requirements for certification.* (1) The requirements for certification for chloramphenicol ophthalmic are described under § 455.310b of this chapter.

(2) When it is intended solely for veterinary use, its label and labeling shall comply with all the requirements of § 455.310b(a)(3) of this chapter, except that in lieu of the statement "Caution: Federal law prohibits dispensing without prescription", it shall be labeled in accordance with the requirements prescribed by § 201.105 of this chapter (regulations issued under section 502(f) of the Act).

(b) *Tests and methods of assay.* The tests and methods of assay for chloramphenicol ophthalmic are described in § 455.310b of this chapter.

§ 555.310b Chloramphenicol topical.

(a) *Requirements for certification.* (1) The requirements for certification for chloramphenicol topical are described under § 455.410(a) of this chapter.

(2) When it is intended solely for veterinary use, its label and labeling shall comply with all the requirements of § 455.410(a)(3) of this chapter, except that in lieu of the statement, "Caution: Federal law prohibits dispensing without prescription", it shall be labeled in accordance with the requirements of § 201.105 of this chapter (regulations issued under section 502(f) of the Act) and bear on its label and labeling the statement, "Warning—Not for use in animals which are raised for food production."

(b) *Tests and methods of assay.* The tests and methods of assay for chloramphenicol topical are described under § 455.410(b) of this chapter.

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§ 555.310c Chloramphenicol ophthalmic ointment.

(a) *Requirements for certification.* The requirements for certification for chloramphenicol ointment (chloramphenicol cream) are described under § 455.310c(a) of this chapter.

(b) *Tests and methods of assay.* The tests and methods of assay for chloramphenicol ointment are described under § 455.310c(b) of this chapter.

(c) *Conditions of marketing—(1) Specifications.* The product conforms to the specification requirements in paragraph (a) of this section, and is subject to the tests and methods of assay prescribed in paragraph (b) of this section. Each gram of the product contains 10 milligrams chloramphenicol.

(2) *Sponsor.* See Nos. 000856 and 025463 in § 510.600(c) of this chapter for use in accordance with paragraph (c)(3)(i)(a) of this section and No. 017030 for use in accordance with paragraph (c)(3)(i)(b) of this section.

(3) *Conditions of use.* (i) It is used in dogs and cats for the treatment of bacterial conjunctivitis caused by pathogens susceptible to chloramphenicol as follows:

(a) It is applied every 3 hours around the clock for 48 hours after which night instillations may be omitted. Treatment should be continued for 2 days after the eye appears normal.

(b) It is applied to affected eye four to six times daily for the first 72 hours depending upon the severity of the condition. A small amount of ointment should be placed in the lower conjunctival sac. Continue treatment for 48 hours after eye appears normal.

(ii) Therapy for cats should not exceed 7 days. Prolonged use in cats may produce blood dyscrasias. If improvement is not noted in a few days a change of therapy should be considered. When infection is suspected as the cause of a disease process, especially in purulent or catarrhal conjunctivitis, attempts should be made to determine through susceptibility testing, which antibiotics will be effective prior to applying ophthalmic preparations. This chloramphenicol product must not be used in animals producing

neat, eggs, or milk. The length of time that residues persist in milk or tissues has not been determined.

(iii) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

10 FR 13036, Mar. 27, 1975, as amended at 53 FR 3838, Jan. 21, 1977; 53 FR 23390, June 2, 1988

555.310d Chloramphenicol ophthalmic solution.

(a) *Requirements for certification—*

(i) *Standards of identity, strength, quality, and purity.* Chloramphenicol ophthalmic solution contains in each milliliter 5 milligrams of chloramphenicol with or without one or more suitable and harmless preservatives and surfactants in an aqueous solution. Its potency is not less than 90 percent and not more than 130 percent of the number of milligrams of chloramphenicol that it is represented to contain. It is sterile. Its pH is not less than 3 nor more than 6. The chloramphenicol used conforms to the standards prescribed by § 455.10(a)(1) of this chapter.

(2) *Labeling.* It shall be labeled in accordance with the requirements of paragraph (c) of this section and § 10.55 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The chloramphenicol used in making the batch for potency, pH, specific rotation, melting range, absorptivity, and crystallinity.

(b) The batch for potency, sterility, and pH.

(ii) *Samples required:*

(a) The chloramphenicol used in making the batch: 10 containers, each containing not less than 300 milligrams.

(b) The batch:

(1) For all tests except sterility: A minimum of five immediate containers.

(2) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay—*(1) *Potency.* Use either of the following

methods; however, the results obtained from the microbiological turbidimetric assay shall be conclusive.

(i) *Microbiological turbidimetric assay.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Dilute an accurately measured representative portion of the sample in distilled water to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with distilled water to the reference concentration of 2.5 micrograms of chloramphenicol per milliliter (estimated).

(ii) *Spectrophotometric assay.* Dilute a 1-milliliter aliquot of the sample in sufficient distilled water to make a solution containing 20 milligrams of chloramphenicol per milliliter. Dissolve an accurately weighed portion of the working standard in sufficient distilled water to give a solution containing 20 milligrams per milliliter. Warm if necessary to hasten solution of the working standard. Cool. Using a suitable spectrophotometer and distilled water as the blank, determine the absorbance of the sample and standard solutions at 278 nanometers. Calculate the potency of the sample as follows:

Milligrams of chloramphenicol per milliliter =

$$\frac{\text{Absorbance of sample} \times \text{labeled potency per milliliter in milligrams}}{\text{Absorbance of standard}}$$

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *pH.* Proceed as directed in § 436.202 of this chapter, using the undiluted solution.

(c) *Conditions of marketing—*(1) *Specifications.* The solution conforms to the certification requirements of paragraph (a) of this section. The solution contains as active ingredient, chloramphenicol 0.5 percent with chlorbutanol 0.5 percent as a preservative.

(2) *Sponsor.* See No. 017030 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) It is used in dogs and cats for the treatment of bac-

terial conjunctivitis caused by organisms susceptible to chloramphenicol.

(ii) Treat with one or two drops, 4 to 6 times a day for the first 72 hours, depending upon the severity of the condition. Intervals between applications may be increased after the first 2 days. Therapy should be continued for 48 hours after an apparent cure has been attained.

(iii) Therapy for cats should not exceed 7 days. As with other antibiotics, prolonged use may result in overgrowth of nonsusceptible organisms. If superinfection occurs, or if clinical improvement is not noted within a reasonable period, discontinue use, and institute appropriate therapy. Prolonged use in cats may produce blood dyscrasias. This chloramphenicol product must not be used in meat, egg-, or milk-producing animals. The length of time that residues persist in milk or tissues has not been determined.

(iv) For use by or on the order of a licensed veterinarian.

(Secs. 507, 512(n), 701 (f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371 (f) and (g)))

[40 FR 13938, Mar. 27, 1975, as amended at 48 FR 3962, Jan. 28, 1983; 50 FR 19923, May 13, 1985]

§ 555.310e Chloramphenicol-prednisolone-tetracaine-squalane topical suspension.

(a) *Requirements for certification—*

(1) *Standards of identity, strength, quality, and purity.* This drug is a suspension composed of chloramphenicol, prednisolone, tetracaine, and squalane in a suitable and harmless vehicle. Each milliliter contains 4.2 milligrams of chloramphenicol, 1.7 milligrams of prednisolone, 4.2 milligrams of tetracaine, and 0.21 milliliter of squalane. Its moisture content is not more than 1 percent. Its antibiotic potency is not less than 90 percent and not more than 125 percent of the number of milligrams of chloramphenicol that it is represented to contain. The chloramphenicol used conforms to the standards prescribed by § 455.10(a)(1) of this chapter.

(2) *Labeling.* It shall be labeled in accordance with the requirements of

paragraph (c) of this section and § 510.55 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The chloramphenicol used in making the batch for potency, pH, specific rotation, melting range, absorptivity, and crystallinity.

(b) The batch for potency and moisture.

(ii) *Samples required:*

(a) The chloramphenicol used in making the batch: 10 containers, each containing approximately 300 milligrams.

(b) The batch: A minimum of six immediate containers.

(b) *Tests and methods of assay—(1)*

Potency. Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Transfer an accurately measured portion of the sample into a separatory funnel containing 50 milliliters of petroleum ether. Shake the separatory funnel vigorously to bring about complete mixing of the sample and the petroleum ether. Add 20 milliliters of distilled water and shake well. Remove the aqueous layer and repeat the extraction with three additional 20-milliliter portions of distilled water. Combine the extractives and dilute to an appropriate volume with distilled water. Further dilute an aliquot with distilled water to the reference concentration of 2.5 micrograms of chloramphenicol per milliliter (estimated).

(2) *Moisture.* Proceed as directed in § 436.201 of this chapter, using 1 or 2 milliliters of the suspension.

(c) *Conditions of marketing—(1)*

Specification. The suspension conforms to the certification requirements of paragraph (a) of this section. Each cubic centimeter of suspension contains 4.2 milligrams of chloramphenicol, 1.7 milligrams of prednisolone, 4.2 milligrams of tetracaine, and 0.21 milliliter of squalane in a petroleum-mineral oil base.

(2) *Sponsor.* See No. 017030 in § 510.600(c) of this chapter.

(3) *Conditions of use.* It is used in the treatment of acute otitis externa and pyoderma (acute moist dermatitis).

tis, vulvar fold dermatitis, lip fold dermatitis, interdigital dermatitis, and juvenile dermatitis) in dogs and cats. Laboratory tests should be conducted, including *in-vitro* culturing and susceptibility tests on samples collected prior to treatment. Treat with two or three applications daily or as needed for not more than 7 days. Severe infections should be supplemented by systemic therapy. The drug must not be used in the eyes. Prolonged use in cats may produce blood dyscrasias. Chloramphenicol products must not be used in meat, egg, or milk producing animals. The length of time that residues persist in milk or tissues has not been determined. For use by or on the order of a licensed veterinarian.

(Secs. 507, 512(n), 701 (f) and (g), 52 Stat. 1055-1056 as amended, 59 Stat. 463 as amended, 82 Stat. 350-351 (21 U.S.C. 357, 360b(n), 371 (f) and (g)))

(40 FR 13938, Mar. 27, 1975, as amended at 48 FR 3962, Jan. 28, 1983; 48 FR 7440, Feb. 22, 1983; 50 FR 19923, May 13, 1985)

§ 555.310f Chloramphenicol-prednisolone ophthalmic ointment.

(a) *Requirements for certification.* The requirements for certification for chloramphenicol-prednisolone ophthalmic ointment are described under § 555.310c.

(b) *Tests and methods of assay.* The tests and methods of assay for chloramphenicol-prednisolone ophthalmic ointment are described under § 555.310c.

(c) *Conditions of marketing—(1) Specifications.* The product conforms to the specification requirements in § 555.310c(a) of this chapter and is subject to the tests and methods of assay prescribed in § 555.310c(b) of this chapter. Each gram of the product contains the following active ingredients: 10 milligrams of chloramphenicol and 2.5 milligrams of prednisolone acetate.

(2) *Sponsor.* See No. 017030 in § 510.600(c) of this chapter.

(3) *Conditions of use.* (i) It is used in dogs and cats for the treatment of bacterial conjunctivitis and ocular inflammation caused by organisms susceptible to chloramphenicol.

(ii) It is applied to the affected eye 4 to 6 times daily for the first 72 hours

depending upon the severity of the condition. Continue treatment for 48 hours after an apparent cure has been attained.

(iii) Therapy for cats should not exceed 7 days, prolonged use in cats may produce blood dyscrasia. As with other antibiotics, prolonged use may result in overgrowth of nonsusceptible organisms. If superinfection occurs or if clinical improvement is not noted within a reasonable period, discontinue use and institute appropriate therapy. All topical ophthalmic preparations containing corticosteroids, with or without an antimicrobial agent, are contraindicated in the initial treatment of corneal ulcers. They should not be used until the infection is under control and corneal regeneration is well under way. This chloramphenicol product must not be used in meat, egg-, or milk-producing animals. The length of time that residues persist in milk or tissues has not been determined.

(iv) For use only by or on the order of a licensed veterinarian.

(40 FR 13938, Mar. 27, 1975, as amended at 44 FR 7131, Feb. 6, 1979)

Subpart D—Otic Dosage Forms

§ 555.410 Chloramphenicol otic.

The requirements for certification and the tests and methods of assay for chloramphenicol otic are described under § 555.310b.

PART 556—TOLERANCES FOR RESIDUES OF NEW ANIMAL DRUGS IN FOOD

Subpart A—General Provisions

Sec.

556.1 General considerations; tolerances for residues of new animal drugs in food.

Subpart B—Specific Tolerances for Residues of New Animal Drugs

556.20	2-Acetylaminio-5-nitrothiazole.
556.30	Aklomide.
556.38	Amoxicillin.
556.40	Ampicillin.
556.50	Amprolium.
556.52	Apramycin.
556.60	Arsenic.

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556.70	Bacitracin.
556.90	Buquinolate.
556.100	Carbadox.
556.110	Carbomycin.
556.113	Ceftiofur.
556.115	Cephapirin.
556.120	Chlorhexidine.
556.140	Chlorobutanol.
556.150	Chlortetracycline.
556.160	Clopidol.
556.163	Cloxacillin.
556.165	Cloxacillin.
556.170	Decoquinolate.
556.180	Dichlorvos.
556.200	Dihydrostreptomycin.
556.220	3,5-Dinitrobenzamide.
556.230	Erythromycin.
556.250	Estradiol monopalmitate.
556.260	Ethopabate.
556.270	Ethylenediamine.
556.275	Fenbendazole.
556.277	Fenprostalene.
556.290	Furazolidone.
556.300	Gentamicin sulfate.
556.308	Halofuginone hydrobromide.
556.310	Haloxon.
556.320	Hydrocortisone.
556.330	Hygromycin B.
556.344	Ivermectin.
556.347	Lasalocid.
556.350	Levamisole hydrochloride.
556.360	Lincomycin.
556.375	Maduramicin ammonium.
556.380	Melengestrol acetate.
556.390	Methylparaben.
556.400	Methylprednisolone.
556.410	Metoserpate hydrochloride.
556.420	Monensin.
556.425	Morantel tartrate.
556.428	Narasin.
556.430	Neomycin.
556.440	Nequinolate.
556.445	Nicarbazin.
556.460	Novobiocin.
556.470	Nystatin.
556.480	Oleandomycin.
556.490	Ormetoprim.
556.500	Oxytetracycline.
556.510	Penicillin.
556.520	Prednisolone.
556.530	Prednisone.
556.540	Progesterone.
556.550	Propylparaben.
556.560	Pyrantel tartrate.
556.580	Robenidine hydrochloride.
556.590	Salicylic acid.
556.600	Spectinomycin.
556.610	Streptomycin.
556.620	Sulfabromomethazine sodium.
556.625	Sodium sulfachloropyrazine monohydrate.
556.630	Sulfachlorpyridazine.
556.640	Sulfadimethoxine.
556.650	Sulfathoxypyridazine.
556.660	Sulfamerazine.

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556.670	Sulfamethazine.
556.680	Sulfantran.
556.690	Sulfathiazole.
556.700	Sulfomycin.
556.710	Testosterone propionate.
556.720	Tetracycline.
556.730	Thiabendazole.
556.738	Tiamulin.
556.739	Trenbolone.
556.740	Tylosin.
556.750	Virginiamycin.
556.760	Zeranol.
556.770	Zoalene.

AUTHORITY: Sec. 512, 82 Stat. 343-3 U.S.C. 360b); 21 CFR 5.10 and 5.83.

SOURCE: 40 FR 13942, Mar. 27, 1975, otherwise noted.

Subpart A—General Provisions

§ 556.1 General considerations; tolerances for residues of new animal drugs in food.

(a) Tolerances established in this part are based upon residues of drugs in edible products of food-producing animals treated with such drugs. Consideration of an appropriate tolerance for a drug shall result in a conclusion either that:

(1) Finite residues will be present in the edible products—in which case a finite tolerance is required; or

(2) It is not possible to determine whether finite residues will be present but there is reasonable expectation that they may be present in which case a tolerance for negligible residue is required; or

(3) The drug induces cancer when ingested by man or animal or, after excretion, which are appropriate for the evaluation of the safety of such drug has been shown to induce cancer in man or animal; however, such drug will not adversely affect the animals for which it is intended, and no residue of the drug will be found by prescribed methods of analysis in any edible portion of such animals after slaughter or in any food yielded by or derived from such living animal—in which case the accepted method of analysis shall be published or cited, if previously published and available elsewhere, in this part; or

(4) It may or may not be possible to determine whether finite residues

be incurred but there is no reasonable expectation that they may be present—in which case the establishment of a tolerance is not required; or

(5) The drug is such that it may be metabolized and/or assimilated in such form that any possible residue would be indistinguishable from normal tissue constituents—in which case the establishment of a tolerance is not required.

(b) No tolerance established pursuant to paragraph (a)(1) of this section will be set at any level higher than that reflected by the permitted use of the drug.

(c) Any tolerance required pursuant to this section will, in addition to the toxicological considerations, be conditioned on the availability of a practicable analytical method to determine the quantity of residue. Such method must be sensitive to and reliable at the established tolerance level or, in certain instances, may be sensitive at a higher level where such level is also deemed satisfactory and safe in light of the toxicity of the drug residue and of the unlikelihood of such residue's exceeding the tolerance.

Subpart B—Specific Tolerances for Residues of New Animal Drugs

§ 556.20 2-Acetylamino-5-nitrothiazole.

A tolerance of 0.1 part per million is established for negligible residues of 2-acetylamino-5-nitrothiazole in the edible tissues of turkeys.

§ 556.30 Aklomide.

Tolerances are established for combined residues of aklomide (2-chloro-4-nitrobenzamide) and its metabolite (4-amino-2-chlorobenzamide) in uncooked edible tissues of chickens as follows:

- (a) 4.5 parts per million in liver and muscle.
- (b) 3 parts per million in skin with fat.

§ 556.38 Amoxicillin.

A tolerance of 0.01 part per million is established for negligible residues of amoxicillin in milk and in the uncooked edible tissues of cattle.

[49 FR 45422, Nov. 16, 1984]

§ 556.40 Ampicillin.

A tolerance of 0.01 p/m is established for negligible residues of ampicillin in the uncooked edible tissues of swine and cattle and in milk.

§ 556.50 Amprolium.

Tolerances are established as follows for residues of amprolium (1-(4-amino-2-n-propyl-5-pyrimidinylmethyl)-2-picolinium chloride hydrochloride):

(a) In the edible tissues and in eggs of chickens and turkeys:

(1) 1 part per million in uncooked liver and kidney.

(2) 0.5 part per million in uncooked muscle tissue.

(3) In eggs:

(i) 8 parts per million in egg yolks.

(ii) 4 parts per million in whole eggs.

(b) In the edible tissues of calves:

(1) 2.0 parts per million in uncooked fat.

(2) 0.5 part per million in uncooked muscle tissue, liver, and kidney.

(c) In the edible tissues of pheasants:

(1) 1 part per million in uncooked liver.

(2) 0.5 part per million in uncooked muscle.

[40 FR 13942, Mar. 27, 1975, as amended at 50 FR 18472, May 1, 1985]

§ 556.52 Apramycin.

Tolerances of 0.1 part per million are established for total residues of apramycin in uncooked swine muscle, 0.3 part per million for liver, and 0.4 part per million for kidney and fat. A drug residue assay measuring parent apramycin (the marker residue) in the target tissue, kidney, serves to monitor the total residue in edible tissues. A marker residue concentration of 0.1 part per million in kidney corresponds to 0.4 part per million total residue in this target tissue.

[47 FR 15771, Apr. 13, 1982]

§ 556.60 Arsenic.

Tolerances for total residues of combined arsenic (calculated as As) in food are established as follows:

(a) In edible tissues and in eggs of chickens and turkeys:

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- (1) 0.5 part per million in uncooked muscle tissue.
- (2) 2 parts per million in uncooked edible by-products.
- (3) 0.5 part per million in eggs.
- (b) In edible tissues of swine:
 - (1) 2 parts per million in uncooked liver and kidney.
 - (2) 0.5 part per million in uncooked muscle tissue and by-products other than liver and kidney.

§ 556.70 Bacitracin.

Tolerances for residues of bacitracin from zinc bacitracin or bacitracin methylene disalicylate are established at 0.5 part per million (0.02 unit per gram), negligible residue, in uncooked edible tissues of cattle, swine, chickens, turkeys, pheasants, and quail, and in milk and eggs.

[42 FR 18614, Apr. 8, 1977]

§ 556.90 Buquinolate.

Tolerances are established for residues of buquinolate as follows:

- (a) In edible tissues of chickens:
 - (1) 0.4 part per million in uncooked liver, kidney, and skin with fat.
 - (2) 0.1 part per million in uncooked muscle.
- (b) In eggs:
 - (1) 0.5 part per million in uncooked yolk.
 - (2) 0.2 part per million in uncooked whole eggs.

§ 556.100 Carbadox.

No residues of carbadox (Methyl 3-(2-quinoxalinylmethylene) carbazate-*N'*, *N'*-dioxide) and its metabolite (quinoxaline-2-carboxylic acid) are found in the uncooked edible tissues of swine as determined by the following method of analysis:

I. REAGENTS

- A. Benzene—Distilled-in-Glass grade, Burdick and Jackson Laboratories or equivalent.
- B. Ethyl acetate—Distilled-in-Glass grade, Burdick and Jackson Laboratories or equivalent.
- C. n-Hexane—Distilled-in-Glass grade, Burdick and Jackson Laboratories or equivalent.
- D. 1-Propanol—reagent grade, dried over molecular sieve pellets (5A).
- E. Citric acid monohydrate—U.S.P., Pfizer, Inc., or equivalent.

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- F. Potassium hydroxide—pellets, reagent grade.
- G. Sodium hydroxide—pellets, reagent grade.
- H. Hydrochloric acid—reagent, A.C.S.
- I. Sulfuric acid—reagent, A.C.S.
- J. Sodium sulfate—anhydrous, reagent grade.
- K. Quinoxaline-2-carboxylic acid—Pfizer, Inc., or equivalent.
- L. Propyl quinoxaline-2-carboxylate—Pfizer, Inc., or equivalent.
- M. Acridine—practical grade; Matheson Coleman and Bell or equivalent.

II. SOLUTIONS

- A. 1*M* Citric acid.
- B. 5*M* Sodium hydroxide.
- C. 3*M* Potassium hydroxide.
- D. 0.5*M* Citric acid buffer. Adjust the pH of 100 milliliters of 1*M* citric acid to pH 6.0 with 5*M* sodium hydroxide (approximately 55 milliliters), using a previously calibrated pH meter. Adjust the final volume to 200 milliliters with distilled water. Before making the final pH adjustment, cool the buffer to room temperature.
- E. 1-Propanol-sulfuric acid reagent (97:3). Dilute 3 milliliters of concentrated sulfuric acid to 100 milliliters with dried, filtered, and cooled 1-propanol.
- F. Acridine solution. Dissolve 1 milligram of acridine in 100 milliliters of benzene.
- G. Quinoxaline-2-carboxylic acid solutions:
 1. Stock solution A. Dissolve 1.25 milligram of quinoxaline-2-carboxylic acid in enough 1-propanol to make 100.0 milliliters (concentration 12.5 micrograms per milliliter).
 2. Stock solution B. Dilute 1.0 milliliter of stock solution A to 100.0 milliliters with 1-propanol-sulfuric acid reagent (concentration 0.125 microgram per milliliter).
 3. Working standard solution C. Dilute a 2.0 milliliter aliquot of stock solution B to 10.0 milliliters with 1-propanol-sulfuric acid reagent (concentration 25.0 nanograms per milliliter).
 4. Working standard solution D. Dilute a 3.0 milliliter aliquot of stock solution B to 10.0 milliliters with 1-propanol-sulfuric acid reagent (concentration 37.5 nanograms per milliliter).
 5. Working standard solution E. Dilute a 4.0 milliliter aliquot of stock solution B to 10.0 milliliters with 1-propanol-sulfuric acid reagent (concentration 50.0 nanograms per milliliter).
 6. Fortification solution. Dilute 3.0 milliliters stock solution A to 250 milliliters with distilled water (concentration 150 nanograms per milliliter).
 7. Propyl quinoxaline-2-carboxylate solution. Dissolve 1.00 milligram of propyl quinoxaline-2-carboxylate in enough ethyl ace-

take to make 10 milliliters (concentration 100 micrograms per milliliter).

III. APPARATUS

A. Column, glass-tapered at one end, 0.9 centimeters x 21.5 centimeters, prepared from a 10-milliliter serological pipette.

B. Centrifuge tubes, heavy duty—50-milliliter graduated (60-milliliter capacity), equipped with glass stoppers, R. C. Ewald, Inc. or equivalent.

C. Centrifuge tubes—50-milliliter graduated, equipped with glass stoppers.

D. Volumetric flasks—5 10 100 and 250-milliliter capacity, glass stoppered.

E. Pipettes, automatic transfer—10 15 and 25-milliliter delivery volume.

F. Pipettes, measuring—0.1 and 0.5 milliliter delivery volume.

G. Pipettes, volumetric—1 2 3 4 and 5-milliliter delivery volume.

H. Pipette, serological—10 milliliter delivery volume.

I. Pipettes—Pasteur, disposable.

J. Propipette bulb.

K. Syringe—10 microliter capacity, Hamilton or equivalent.

L. Crystallizing dish—190 millimeter (diameter) x 100 millimeter (height), for oil bath.

M. Test tube rack.

N. Test tube mixer—Vortex mixer or equivalent.

O. Lab jack—Cenco or equivalent.

P. Thermo-stir hotplate.

Q. Magnetic stirrer bar (teflon).

R. Thermometer—centigrade, 0° to 150° C. range.

S. Knife (for cutting frozen tissue).

T. Ultraviolet light—254 nanometers and 366 nanometers.

U. Scalpel.

V. Torsion balance—style RX-1, class A, Torsion Balance Co., or equivalent.

W. Cahn electrobalance—Cahn Model C-2 or equivalent.

X. Centrifuge—International, size 2, model K, or equivalent.

Y. Rotary evaporator equipped either with a water aspirator or with a vacuum pump and condenser.

Z. Alkacid test paper.

AA. Glassine paper.

BB. Glasswool.

CC. Flask—round bottom, 29/42 ST, 250 milliliters.

DD. Flask—round bottom, 19/22 ST, 65 milliliters.

EE. Funnel—burette.

FF. Hair dryer.

GG. pH meter.

HH. Tray—instrument, stainless steel.

II. Water bath.

JJ. Precoated thin layer plates—20 x 20 centimeters; 250 micron thickness, Silica gel

OP, E. Merck, Darmstadt; distributed by

Brinkmann Instruments Inc., Westbury, N.Y. 11590 or equivalent.

KK. Desaga multiplate developing tanks for five 20 x 20 centimeters plates—distributed by Brinkmann Instruments Inc., or equivalent.

LL. Gas-liquid chromatograph—Micro Tek 220 model instrument (or equivalent) equipped with a Ni⁶³ electron affinity pulsed detector and a 0-1 MV recorder. Conditions and operating parameters for the gas-liquid chromatograph are: Isothermal column temperature, 175° C.; inlet heater, 270° C.; EC detector temperature, 275° C.; argon-methane (95:5) flowrate, 100 milliliters per minute (40 pounds per square inch); chart speed, 1/4 inch per minute, attenuation, 10 x 64. Electrometer pulse parameters: RF mode; voltage output, 55; pulse rate, 270 microseconds; pulse width, 3.0 microseconds.

A glass sleeve injection port liner is installed for off-column injections.

MM. Packing—3 percent OV-17 on Gas Chrom Q, 60-80 mesh, Applied Sciences Laboratories, Inc. or equivalent.

NN. Column—pyrex glass, U-tube, 6 feet (length) x 4 millimeters (inside diameter). Condition the packed column at 280° C. for at least 72 hours with argon-methane (95:5) flow, detached from the detector input.

OO. Septum—high temperature type (HT-13), Applied Sciences Laboratories, Inc. or equivalent.

PP. Detector—Nickel⁶³ electron capture. The voltage current profile for this detector should plateau at 30 volts or less in the DC mode when a stream of nitrogen gas is passed through the column and the electron capture detector.

IV. PROCEDURE

A. DISSOLUTION AND HYDROLYSIS STEP

Transfer 5 grams of swine tissue (freshly sliced from frozen tissue) to a 50-milliliter centrifuge tube. Add 10 milliliters of 3M potassium hydroxide, stopper, and place in a 100° C. silicone oil bath for 1 hour.

NOTE: The level of the silicone oil bath should exceed that of the tissue sample. Stopper the tubes lightly in order to allow the digestion mixture to "breathe". To determine the recovery of quinoxaline-2-carboxylic acid in swine tissue at the 30 p.p.b. level, fortify 5 grams of sample with 1 milliliter of fortification solution (concentration 150 nanograms per milliliter).

B. EXTRACTION STEP

1. Cool the alkaline hydrolyzate in an ice bath and acidify to 1 pH 1 (deep red to alkacid test paper) with 4 milliliters of concentrated hydrochloric acid. Add 15 milliliters of ethyl acetate to the acidified hydrolyzate, stopper, and extract by shaking for

20 seconds. Centrifuge the mixture at 1,500 revolutions per minute for 5 minutes to clarify the ethyl acetate phase. Recover the ethyl acetate phase with a blowout pipette equipped with a propipette bulb, and transfer this extract to a 60-milliliter separatory funnel equipped with teflon stopcocks. Reextract the hydrolyzate with two additional 15-milliliter portions of ethyl acetate, and combine the organic extracts.

NOTE: Do not contaminate the ethyl acetate phase with interfacial material during these extractions. Quinoxaline-3-carboxylic acid is unstable in strongly acidic solutions. Continue to process these extracts through the benzene extraction and evaporation steps.

2. Add 5 milliliters of 0.5M citric acid buffer (pH 6.0) to the ethyl acetate extract, shake, and allow the lower phase to clarify for about 20 minutes. Collect the aqueous phase in a 50-milliliter glass-stoppered centrifuge tube. Reextract the ethyl acetate phase with an additional 5 milliliters of pH 6 buffer, wait for the aqueous phase to clarify, and combine the aqueous extracts. Acidify (pH 1) the aqueous extract with 2 milliliters of concentrated hydrochloric acid, stopper, and extract with 25 milliliters of benzene. Centrifuge to clarify the benzene layer and transfer the organic phase, using a blowout pipette equipped with a propipette bulb, to a 250-milliliter round bottom flask. Repeat the extraction and centrifugation steps three times. Combine the benzene extracts (about 100 milliliters) and evaporate to near-dryness, using a rotary evaporator equipped with a water aspirator and with a water bath set at 40° C.

NOTE: A rotary evaporator equipped with a vacuum pump and condenser may be used at this point. These residues may be stored overnight.

C. ESTERIFICATION STEP

Reconstitute the residue from the previous step by rinsing the walls of the round bottom flask with 2 x 2 milliliters of 1-propanol-sulfuric acid reagent; transfer each rinse with a disposable pipette to a 50-milliliter centrifuge tube. Stopper and heat the tube in a silicone oil bath at 90° C. for 1 hour. Cool the reaction mixture in an ice bath before proceeding to the following extraction step.

NOTE: Samples and standards may be stored overnight at room temperature in the propanol-sulfuric acid medium.

D. EXTRACTION OF THE ESTER DERIVATIVE

Add 10 milliliters of water and 15 milliliters of n-hexane to the esterification mixture. Extract and centrifuge to clarify the n-hexane phase. Transfer the n-hexane extract to a 65-milliliter round bottom flask;

reextract the aqueous-propanol phase with two additional 15-milliliter portions of n-hexane. Centrifuge after each extraction and combine the n-hexane extracts. (**NOTE:** Avoid taking any of the aqueous phase in this extraction step; otherwise, the n-hexane extracts will have to be washed with 3 x 10 milliliters of water and dried over sodium sulfate.) Concentrate this solution to 0.5 milliliter, using a rotary evaporator equipped with a water aspirator and with a water bath set at 25° C. (**NOTE:** A rotary evaporator equipped with a vacuum pump and condenser may be used at this point.) Fortify this solution with 0.1 milliliter of acridine marker (1 milligram per 100 milliliters benzene).

NOTE: Do not store the n-hexane extract of the propyl ester derivative overnight. Continue to process these solutions by the following thin-layer chromatography step E.

E. THIN-LAYER CHROMATOGRAPHY

1. Quantitatively transfer the concentrated n-hexane extract to the "origin" of a 30 centimeters x 20-centimeters silica gel thin-layer plate, using a disposable pipette. When pipetting this extract, streak it in a uniform band approximately 15 centimeters across and approximately 20 millimeters above the lower edge of the plate, making sure not to scratch or remove appreciable portions of adsorbent and avoiding application of the sample to the sides of the plate. The applied band should not diffuse or penetrate to the end of the silica gel layer, but should remain 10 millimeters above the lower edge of the silica gel layer. Rinse the round bottom flask (containing residual n-hexane) with three portions of approximately 0.25 milliliter each of ethyl acetate; transfer each portion with the same pipette and cover the same area of the plate as described above. Following each application of the extract and ethyl acetate washes, evaporate the solvent from the plate by directing a stream of cool air to the sample zone ("origin"). Prior to chromatographic development, place an edge (approximately 5 millimeters deep) of the thin-layer plate into a tray of ethyl acetate so that the solvent will rise through the applied sample zone to form it into a narrow band approximately 10 millimeters above the "origin." Air dry this plate before chromatographic development.

2. Place the prepared plate in a chromatographic chamber lined with blotting paper and saturated with the benzene-ethyl acetate system (85:15). Develop the plate twice in this system, maintaining straight solvent fronts and allowing the solvent front to reach the top of the plate during each migration. Air dry the thin-layer plate for 24

approximately 5 minutes between the first and second irrigations. Each irrigation takes approximately 75 minutes. Developed plates should not be stored overnight. Examine the developed plate under long wavelength (366 nanometers) ultraviolet light and locate the blue fluorescent band of acridine (R_f approximately 0.5). Mark out a 12-millimeter x 20-centimeter band of silica gel encompassing an area 5 millimeters above and 7 millimeters below the center of the acridine marker and extending from one side of the plate to the other.

NOTE: The relative mobilities of propyl quinoxaline-2-carboxylate and acridine must be checked in each laboratory to determine where a 12-millimeter x 20-centimeter zone of silica gel is to be excised in order to quantitatively recover the propyl ester derivative. This may be accomplished by mixing 0.1 milliliter of acridine solution (1 milligram per 100 milliliters) with 0.4 milliliter of propyl quinoxaline-2-carboxylate (100 micrograms per milliliter) and chromatographing this solution as directed above. Examine the developed plate under long wavelength (366 nanometers) ultraviolet light and locate the blue fluorescent band of acridine (R_f approximately 0.5). Examination of the plate under short wavelength (254 nanometers) ultraviolet light locates the blue absorbing band of propyl quinoxaline-2-carboxylate (R_f approximately 0.5).

2. Reduce the sample zone to a fine powder by making a series of horizontal cuts with a scalpel. Gently transfer this powder with the aid of a stainless steel spatula to glassine paper; pour this material into a burette funnel atop a small glass column packed with a glass wool plug. Elute the adsorbent with ethyl acetate (about 6 milliliters), and collect the eluate to mark in a 5-milliliter volumetric flask. Examine this eluate by gas-liquid chromatography.

NOTE: Contamination of thin-layer chromatographic plates can be checked by gas-liquid chromatographic examination of an eluate prepared by processing a blank plate as in paragraph 1 above, starting at the point: "place an edge (approximately 5 millimeters deep) of the thin-layer plate into a tray of ethyl acetate" If the plate is contaminated, examine alternate lots of pre-coated thin-layer plates.

F. STANDARD CURVE

Pipette 4-milliliter aliquots of quinoxaline-2-carboxylic acid working standard solutions C, D, and E, respectively, and 4-milliliter portions of 1-propanol-sulfuric acid reagent into 50-milliliter centrifuge tubes; stopper, react, extract, and concentrate as directed in the esterification and extraction steps described in subsections C and D above; however, omit the addition of acridine to the n-hexane concentrate and do not

chromatograph it by thin-layer chromatography. Instead, reconstitute the n-hexane concentrate with ethyl acetate and quantitatively transfer this solution to a 5-milliliter volumetric flask to give working standard solutions C, D, and E. The final concentrations of working standard solutions C, D, and E, are 20, 30, and 40 nanograms per milliliter, respectively, and are equivalent to 20, 30, and 40 p.p.b., respectively.

G. GAS-LIQUID CHROMATOGRAPHY

Separately inject 4 microliters of each of the working standard solutions C, D, and E (prepared as described above (F)) into the gas-liquid chromatograph to determine the retention time of propyl quinoxaline-2-carboxylate and the relative response of the EC detector. Construct a standard curve by plotting concentration (p.p.b.) versus peak height (millimeters).

NOTE: The reagent blank must show no interfering gas-liquid chromatographic peaks. The peak height of propyl quinoxaline-2-carboxylate at the 30-p.p.b. level (working standard solution D) should approximate 10 percent of full-scale deflection with a retention time of 5 minutes. Follow these injections with 4-microliter injections of the tissue eluates, allowing 20 minutes between injections to clear the instrument of background peaks.

Measure the peak heights of samples and determine their concentration (p.p.b.) by reference to the standard curve.

H. CALCULATIONS

From the standard curve and the observed peak height of quinoxaline-2-carboxylic acid in the sample, determine its concentration (p.p.b.).

§ 556.110 Carbomycin.

A tolerance of zero is established for residues of carbomycin in the uncooked edible tissues of chickens.

§ 556.113 Ceftiofur.

A tolerance for a marker residue of ceftiofur in cattle tissue is not needed. The safe concentrations for total residues of ceftiofur in uncooked edible tissues of cattle are: 3.0 parts per million muscle, 9.0 parts per million kidney, 6.0 parts per million liver, 12.0 parts per million fat. "Tolerance" refers to a concentration of a marker residue in a target tissue selected to monitor for total residues of the drug in the target animal. "Safe concentration" refers to the concentrations of

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total residues considered safe in edible tissues.

[53 FR 5370, Feb. 24, 1988]

§ 556.115 Cephapirin.

A tolerance of 0.02 parts per million (ppm) is established for residues of cephalapirin in the milk and 0.1 ppm in the uncooked edible tissues of dairy cattle.

[40 FR 57454, Dec. 10, 1975]

§ 556.120 Chlorhexidine.

A tolerance of zero is established for residues of chlorhexidine in the uncooked edible tissues of calves.

§ 556.140 Chlorobutanol.

A tolerance of zero is established for residues of chlorobutanol in milk from dairy animals.

§ 556.150 Chlortetracycline.

Tolerances are established for residues of chlortetracycline in food as follows:

(a) In edible tissues and in eggs of chickens, turkeys, and ducks:

(1) 4 parts per million in uncooked kidney.

(2) 1 part per million in uncooked muscle, liver, fat, and skin.

(3) Zero in eggs.

(b) In edible tissues of swine:

(1) 4 parts per million in uncooked kidney.

(2) 2 parts per million in uncooked liver.

(3) 1 part per million in uncooked muscle.

(4) 0.2 part per million in uncooked fat.

(c) In edible tissues of calves:

(1) 4 parts per million in uncooked liver and kidney.

(2) 1 part per million in uncooked muscle and fat.

(d) In edible tissues of beef cattle and nonlactating dairy cows:

(1) 0.1 part per million in uncooked kidney, liver, and muscle.

(2) Zero in uncooked fat.

(e) Zero in milk.

(f) In edible tissues of sheep:

(1) 1 part per million in uncooked kidney.

(2) 0.5 part per million in uncooked liver.

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(3) 0.1 part per million in uncooked muscle.

[40 FR 13942, Mar. 27, 1975, as amended at 49 FR 23634, May 31, 1984]

§ 556.160 Clopidol.

Tolerances for residues of clopidol (3,5-dichloro-2,6-dimethyl-4-pyridinol) in food are established as follows:

(a) In cereal grains, vegetables, and fruits: 0.2 part per million.

(b) In chickens and turkeys:

(1) 15 parts per million in uncooked liver and kidney.

(2) 5 parts per million in uncooked muscle.

(c) In cattle, sheep, and goats:

(1) 3 parts per million in uncooked kidney.

(2) 1.5 parts per million in uncooked liver.

(3) 0.2 part per million in uncooked muscle.

(d) In swine: 0.2 part per million in uncooked edible tissues.

(e) In milk: 0.02 part per million (negligible residue).

§ 556.163 Clorsulon.

Tolerances are established for residues of clorsulon in cattle as follows:

(a) The tolerance for clorsulon (market residue) in kidney (target tissue) is 1.0 part per million. A marker residue of 1.0 part per million corresponds to a total residue of 3.0 parts per million in kidney.

(b) The safe concentrations for total clorsulon residues in uncooked edible cattle tissues are: muscle, 1.0 part per million; liver, 2.0 parts per million; kidney, 3.0 parts per million; and fat, 4.0 parts per million.

[50 FR 10221, Mar. 14, 1985]

§ 556.165 Cloxacillin.

A tolerance of 0.01 part per million is established for negligible residues of cloxacillin in the uncooked edible tissues of cattle and in milk.

[40 FR 28792, July 9, 1975]

§ 556.170 Decoquinale.

Tolerances for residues of decoquinale in food are established as follows in uncooked edible tissues of chickens, cattle, and goats at 2 parts per million.

in tissues other than skeletal muscle and 1 part per million in skeletal muscle.

(52 FR 43061, Nov. 9, 1987)

§ 556.180 Dichlorvos.

A tolerance of 0.1 part per million is established for negligible residues of dichlorvos (2,2-dichlorovinyl dimethyl phosphate) in the edible tissues of swine.

§ 556.200 Dihydrostreptomycin.

A tolerance of zero is established for residues of dihydrostreptomycin in uncooked edible tissues of calves, in milk from dairy animals, and in any food in which such milk has been used.

§ 556.220 3,5-Dinitrobenzamide.

No residues of 3,5-dinitrobenzamide may be found in the uncooked edible tissues of chickens as determined by the following method of analysis:

I. Method of analysis—3,5-dinitrobenzamide. A method for 3,5-dinitrobenzamide (3,5-DNBA) in chicken tissues is described with a cleanup step that removes most of the interfering materials, thus allowing uncompensated measurements to be read. The 3,5-DNBA is extracted from the sample with acetone and chloroform and prepared for chromatography by removing the aqueous phase in a separatory funnel and the solvent in a flash evaporator. The extract residue is chromatographed on alumina to remove several lipid components and residues of other drugs. The benzamide eluate passed through a column of Dowex-50 resin, or equivalent, to remove arylamines; for example, 3-amino-5-nitrobenzamide. The 3,5-DNBA fraction is reduced, after removal of alcohol, with TiCl_4 in basic solution to an arylamine, presumably 3,5-diaminobenzamide. The reduced fraction is placed on another Dowex-50 column, most of the interfering substances are removed with washings of alcohol and water, and the arylamine residue is eluted with 4N HCl. Colorimetric measurement is made in a 100-milliliter cell at 530 millimicrons after reacting the residue with Bratton-Marshall reagents.

II. Reagents.

A. Acetone.
B. Acetyl-(p-nitrophenyl)-sulfanilamide (PNPS) standard—melting point range 1° C.-267° C. Weigh and transfer 10 milligrams of APNPS to a 100-milliliter flask, dissolve and dilute to volume with acetone.
C. Alumina—activated F-20, 80-200 mesh, Riedel Co. of America, or equivalent substance.
D. Ammonium sulfamate.

E. Ammonium sulfamate solution 1.25 grams of ammonium sulfamate per 100 milliliters of water. Refrigerate when not in use. Prepare fresh weekly.

F. Cation-exchange resin—Dowex 50W-X8, 200-400 mesh, Baker Analyzed Reagent, or equivalent, prepared as follows:

1. Place 500 grams of resin into a 3-liter beaker.

2. Add 2,000 milligrams of 6N HCl.

3. Heat and stir while on a bath at 80° C. for 6 hours. Discontinue heating and continue stirring overnight.

4. Filter the resin on a Buchner funnel (24 cm.) fitted with Whatman No. 1 paper.

5. Wash the resin bed with four 500-milliliter portions of 6N HCl.

6. Wash the resin bed with 500-milliliter portions of deionized water until the effluent has a pH of 5 or higher.

7. Wash the resin bed with three 400-milliliter portions of specially denatured alcohol 3A. Drain thoroughly.

8. Make a slurry of resin in 1,250 milliliters of specially denatured alcohol 3A.

G. Chloroform.

H. Coupling reagent—0.25 gram of N-1-naphthyl-ethylenediamine dihydrochloride per 100 milliliters of water. Refrigerate when not in use. Prepare fresh weekly.

I. 3,5-Dinitrobenzamide (3,5-DNBA standard). Add to boiling specially denatured alcohol 3A until a saturated solution is obtained and treat with activated carbon, filtered and crystallize by cooling to room temperature. The 3,5-DNBA therefrom is treated a second time with activated carbon and then recrystallized three more times from specially denatured alcohol 3A. The third crystallization is washed with diethyl ether and dried in a vacuum desiccator, melting point range 185° C.-186° C.

J. Ethyl alcohol—absolute, A.C.S.

K. Eluting reagent A. The formula and volume required in procedure step V-D is dependent on the adsorptive strength of the Al_2O_3 . For each lot Al_2O_3 , make the following test:

1. Prepare a column (see procedure step V-D for determining formula and volume to eluting reagent A).

2. Transfer 1 milliliter of APNPS standard (100 micrograms per milliliter) in 75 milliliters of chloroform to the column.

3. Wash the column with 100 milliliters of chloroform and discard the eluate.

4. Pass through 100 milliliters of solution consisting of specially denatured alcohol 3A and ethyl alcohol 1:1 (volume to volume). Collect one 50-milliliter and five 10-milliliter portions; these make up the first, second, third, fourth, fifth, and sixth portions of eluate.

5. Place in beakers under a stream of air on a water bath (90° C.) until the solvents are evaporated.

6. Add 10 milliliters of 4N HCl to each, cover with watch glasses and heat (90° C.) for 30 minutes; cool to room temperature.
 7. Add the Bratton-Marshall reagents.
 8. All fractions show a slight color. Note the portion containing the first significant increase in pink color.
 - a. If the color increases in the second, third, or fourth portions of eluate, the formula in procedure step V-D is suitable and, depending on the portion, 45, 55, or 65 milliliters, respectively, should be used in procedure step V-D4. Thereby, the APNPS is retained on the column and the benzamides are eluted.
 - b. If the color increases in the first portion, the eluting strength of the reagent is too strong. Return the test, substituting 1:4 (volume to volume) in procedure step V-D4. If 1:4 (volume to volume) is too strong, rerun with ethyl alcohol in procedure step V-D. If none of these are suitable, another lot of Al₂O₃ should be used.
 - c. If the color increases in the fifth or sixth portion, the eluting strength of the reagent is too weak. Rerun the test, substituting in procedure step V-D4, respectively, 4:1 (volume to volume), specially denatured alcohol 3A: methyl alcohol, 4:1 (volume to volume), until a suitable formula is found. If none of these are suitable, another lot of Al₂O₃ should be used.
 - L. Hydrochloric acid, 4N. Add two volumes of water to one volume of HCl.
 - M. Diatomaceous earth—Hyflo Super Cel, Johns-Manville Co., or equivalent substance.
 - N. N-1-Naphthylethylenediamine dihydrochloride.
 - O. Sodium hydroxide solution, 10N. Dissolve 100 grams of sodium hydroxide in water and dilute to 25 milliliters.
 - P. Sodium nitrite solution—0.25 grams of sodium nitrite per 100 milliliters of water. Refrigerate when not in use. Prepare fresh weekly.
 - Q. Specially denatured alcohol, formula 3A—100 parts of 190-proof ethyl alcohol plus 5 parts of commercial methyl alcohol.
 - R. Titanium(ous) chloride—20 percent solution.
- III. Special apparatus. A. Absorption cells—Beckman No. 75193 matched set of two cylindrical silica cells with 100 millimeter optical length, or equivalent cells.
- B. Autotransformer—type 500B, or equivalent. To regulate speed of mixer.
- C. Centrifuge.
- D. Centrifuge tubes—50-milliliter size with glass stopper.
- E. Chromatography tubes—Corning No. 38400, 20 millimeters × 400 millimeters and having a tapered 29/42 joint with coarse, fritted disc, or equivalent tubes.
- F. Evaporator—vacuum, rotary, thin film.
- G. Ion-exchange column—as described by Thiess et al. in "Determination of 3-amino-5-nitro-o-toluidine (ANOT) in chicken tis-

- sues" published in "Journal of Agricultural and Food Chemistry," volume 9, pages 204 (1961).
- H. Glycerol manostat. For regulating pressure on columns: To Al₂O₃ columns, 15-lb head pressure; to ion-exchange columns, 1-inch head pressure.
- I. Motor speed control. For regulating speed on 1-quart blender.
- J. Volumetric flasks—50 milliliter size, tincture ware.
- K. Mixer—Vortex Jr. Model K-500-1, Scientific Industries, Inc., or equivalent mixer.
- L. One-quart blender.
- M. Water bath (45° C.-50° C.).
- N. Water bath (90° C.).
- IV. Standard curve. A. 1. Weigh 100 milligrams of 3,5-DNBA and transfer to a 100-milliliter volumetric flask with acetone.
2. Dissolve and dilute with acetone to volume.
 3. Dilute 1 milliliter to 100 milliliters.
 4. Add 5.0 milliliters of water to each of six centrifuge tubes.
 5. Add standard to each of the tubes to contain one of the following amounts: 0.1, 0.2, 0.3, 0.5, and 1.0 micrograms of 3,5-DNBA.
- B. Prepare each tube for colorimetric measurement as follows:
1. Place the tube in a hot water bath (90° C.) until 5.0 milliliters remain. Cool to room temperature.
 2. While mixing on Vortex mixer or equivalent, regulated with an autotransformer, add 2 drops of TiCl₄ and 4 drops of 10N NaOH. Continue mixing until chalky white in appearance.
 3. Add 2 milliliters of HCl, mix, and allow to stand for 5 minutes.
 4. Transfer to 50-milliliter volumetric flask and dilute with 4N HCl to 40-45 milliliters.
 5. Cool to 0° C.-5° C. by placing in a freezer or ice bath.
 6. Perform the Bratton-Marshall reaction in subdued light as follows:
 - a. Add 1 milliliter of sodium nitrite reagent, mix, and allow to stand for 1 minute.
 - b. Add 1 milliliter of ammonium sulfamate reagent, mix, and allow to stand for 1 minute.
 - c. Add 1 milliliter of coupling reagent, mix, and allow to stand for 10 minutes.
 - d. Dilute to volume with 4N HCl.
- C. Perform colorimetric measurement at 530 millimicrons as follows:
1. Fill two matched 100-millimeter cells with 4N HCl and place into spectrophotometer.
 2. Adjust dark current.
 3. Adjust to zero absorbance.
 4. Replace acid in cell of sample side of compartment with standard to be measured.
 5. The standard curve should be run five different times. Plot equivalent concentration

tion in tissue versus mean absorbance at each concentration. If computer is available, a better procedure is to calculate the equation of the standard curve by means of least squares.

V. Procedure. A. Extraction. 1. Mince 350 grams of tissue in a 1-quart blending jar for 3 minutes. Use samples obtained from either freshly killed or quickly frozen birds. The latter should be analyzed as soon as thawed. For fibrous meats (for example, muscle, skin) put through a meat grinder before mincing.

2. Weight 100 ± 0.5 grams of each replicate sample in a 150-milliliter beaker. Analyze each sample in triplicate and average the results. Reproducibility of ± 10 percent between such analyses has been obtained.

3. Transfer the sample to a 1-quart blender jar. For kidney and liver tissues, make a slurry with acetone in the weighing beaker. Transfer with several rinses of acetone.

4. Blend the sample for 5 minutes with 250 milliliters of acetone and a 100-milliliter beakerful of diatomaceous earth.

5. Filter through a Buchner funnel containing a wetted Whatman No. 5 filter paper (12.5 cm.) into a 1-liter suction flask.

6. Rinse the blender jar into the funnel with three 25-milliliter portions of acetone.

7. Transfer the pulp and paper from the funnel to the aforementioned blender jar.

8. Add 250 milliliters of chloroform.

9. Blend for 3 minutes.

10. Filter through the aforementioned apparatus of procedure step V-A5. For rapid filtration of skin and blood samples, prepare funnel by adding diatomaceous earth and tamping evenly over paper to a thickness of 3 to 5 millimeters.

11. Rinse the blender jar into the funnel with three 25-milliliter rinses of chloroform.

B. Phasic separation. 1. Pour the combined filtrates into a 1-liter separatory funnel.

2. Rinse the suction flask twice with 25 milliliters of chloroform.

3. Mix the funnel contents by gently rocking and swirling for 30 seconds.

4. Let stand 10 minutes to allow phases to separate.

a. The upper (aqueous) phase (30 to 50 milliliters) is not always emulsion-free. Losses from emulsions have not been significant.

b. If an upper (aqueous) phase does not appear, add an additional 100 milliliters of chloroform and 10 milliliters of water and repeat procedure step V-B3.

5. Withdraw the lower phase into a 1-liter round-bottom flask, and discard upper phase. Withdraw nearly all of the lower phase, let stand for 2 to 3 minutes, then withdraw the remainder.

C. Evaporation. Attach the flask on a thin-film rotary evaporator connected to a vacuum supply, and place in a water bath

maintained at 45°C .– 50°C . until an oily residue remains. Do not overheat the sample or allow to go to dryness.

D. Adsorption chromatography. 1. Prepare a chromatography column using a column with calibrated etchings to indicate appropriate adsorbent and solvent levels as follows:

a. Fill tube to a depth of 60 millimeters with Al_2O_3 .

b. Tap walls gently with hands.

c. Add anhydrous sodium sulfate to an additional depth of 25 millimeters.

d. Wet and wash column with 50 milliliters of chloroform.

i. During chromatography, make each addition to the tube when the liquid level has reached the top of the sodium sulfate layer.

ii. Increase the percolation rates by applying a slight air pressure to the top of the column.

2. Transfer the residue from procedure step V-C to the column with four 15-milliliter rinses of chloroform. Then rinse the walls of the tube and sodium sulfate layer with three 5-milliliter portions of chloroform. Percolation rate: 15 to 25 milliliters per minute. No color from sample should be seen in sodium sulfate layer after final rinse.

3. Wash column with 100 milliliters of chloroform. Discard eluate.

4. Add 75 milliliters of eluting reagent A and collect eluate A in a 250-milliliter beaker for cation-exchange chromatography.

a. Refer to "Eluting reagent A" under "Reagents" (II-K) for determining formula and volume.

b. Percolation rate: 8 to 12 milliliters per minute.

E. Cation-exchange chromatography—No. 1. 1. Prepare an ion-exchange column as follows:

a. Add a uniform slurry of resin to the column to obtain a 4 to 5 centimeter bed depth after settling.

i. Obtain a uniform slurry using a magnetic stirrer. To add the required amount of resin, calibrate the slurry and transfer it with a 10-milliliter pipette to deliver a reproducible volume.

ii. Increase the flow rate to 2 to 4 milliliters per minute by applying air pressure to the column. A glycerol manostat adjusted to 30 inches and attached between an air supply and column provides adequate pressure.

b. Wash the resin with 10 milliliters of eluting reagent A. Discard eluate.

2. Pass eluate A from procedure step V-D4 through the column. Collect in a 250-milliliter beaker.

3. Pass 50 milliliters of specially deaerated alcohol 3A through the column. Combine with the eluate of procedure step V-E2.

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F. Reduction. 1. Place the eluate A fraction from procedure step V-E3 on a hot water bath (90° C.) and evaporate with a stream of air until 5 to 10 milliliters remain. Do not overheat the sample or allow the sample to go to dryness.

2. Transfer to centrifuge tube and rinse beaker three times with 3 milliliters of specially denatured alcohol 3A.

3. Evaporate on a hot water bath (90° C.) under a stream of air until alcohol has evaporated. Do not overheat the sample or allow the sample to go to dryness.

4. Remove the tube from the water bath and immediately add 5.0 milliliters of water.

5. While mixing, add 2 drops of titanium chloride and 4 drops of 10N sodium hydroxide. Continue mixing until greyish color disappears.

a. Mix on Vortex Jr. mixer, or equivalent, regulated with autotransformer.

b. Precipitate of insoluble tissue substances and white titanium salts is present after reduction is complete.

6. Dilute to 50 milliliters with specially denatured alcohol 3A and mix.

7. Centrifuge for 5 minutes at 2,000 r.p.m.

G. Cation-exchange chromatography—No. 2. 1. Prepare resin column by procedure step V-E.

2. Pass the centrifugate of procedure step V-F7 through column. Use three rinses of specially denatured alcohol 3A, each 5 milliliters, to aid in transferring of sample.

3. Pass 50 milliliters of specially denatured alcohol 3A through the column.

4. Pass 50 milliliters of deionized water through the column.

5. Elute arylamine residue from the resin with 40 to 43 milliliters of 4N HCl into a 50-milliliter volumetric flask (actinic ware) for 3,5-DNBA analysis. Avoid direct sunlight. The arylamine has been found to be photosensitive.

H. Color development and measurement. 1. Cool to 0° C.-5° C. by placing in a freezer or ice bath.

2. Perform the Bratton-Marshall reaction in subdued light as follows:

a. Add 1 milliliter of sodium nitrite reagent, mix, and allow to stand for 1 minute.

b. Add 1 milliliter of ammonium sulfamate reagent, mix, and allow to stand for 1 minute.

c. Add 1 milliliter of coupling reagent, mix, and allow to stand for 10 minutes.

d. Dilute to volume with 4N HCl.

3. Perform colorimetric measurement at 530 millimicrons as follows:

a. Fill two matched 100-millimeter cells with 4N HCl and place into instrument.

b. Adjust dark current.

c. Adjust to zero absorbance.

d. Replace acid in cell of sample side of compartment with sample to be measured.

e. Record absorbance observed.

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I. Calculations. Determine parts per billion (observed) from the standard curve.

§ 556.230 Erythromycin.

Tolerances for residues of erythromycin in food are established as follows:

(a) 0.1 part per million (negligible residue) in uncooked edible tissues of swine.

(b) Zero in the uncooked edible tissues of beef cattle and in milk.

(c) 0.025 part per million in uncooked eggs.

(d) 0.125 part per million (negligible residue) in uncooked edible tissues of chickens and turkeys.

§ 556.240 Estradiol benzoate.

No residues of estradiol, resulting from the use of estradiol benzoate, are permitted in excess of the following increments above the concentrations of estradiol naturally present in untreated animals:

(a) In uncooked edible tissues of heifers, steers, and calves:

(1) 120 parts per trillion for muscle.

(2) 480 parts per trillion for fat.

(3) 360 parts per trillion for kidney.

(4) 240 parts per trillion for liver.

(b) In uncooked edible tissues of lambs:

(1) 120 parts per trillion for muscle.

(2) 600 parts per trillion for fat, kidney, and liver.

[49 FR 13873, Apr. 9, 1984]

§ 556.250 Estradiol monopalmitate.

(a) No residues of estradiol monopalmitate may be found in the uncooked edible tissues of chickens.

(b) The method of examination prescribed for the quantitative determination of estradiol monopalmitate is as follows: Incorporate finely ground tissues of the treated chickens in the diet of immature mice and assays by the mouse uterine weight method of E. J. Umberger, G. H. Gass, and J. M. Curtis, 'Design of A Biological Assay Method for the Detection and Estimation of Estrogenic Residues in the Edible Tissues of Domestic Animals Treated with Estrogens,' published in *Endocrinology*, 63:806-814, 1958, which is incorporated by reference. Copies are available from the Bureau

of Foods, Food and Drug Administration, 200 C St. SW., Washington, D.C. 20204, or available for inspection at the Office of the Federal Register, 1100 L St. NW., Washington, D.C. 20408.

[40 FR 13942, Mar. 27, 1975, as amended at 47 FR 9397, Mar. 5, 1982]

§ 556.260 Ethopabate.

Tolerance for residues of ethopabate converted to metaphenetidine are established in the edible tissues of chickens as follows:

(a) 1.5 parts per million in uncooked liver and kidney.

(b) 0.5 part per million in uncooked muscle.

§ 556.270 Ethylenediamine.

A tolerance of zero is established for residues of ethylenediamine in milk.

§ 556.275 Fenbendazole.

(a) *Cattle*. The marker residue selected to monitor for total residues of fenbendazole in cattle is parent fenbendazole and the target tissue selected is liver. A tolerance¹ is established in cattle of 0.8 part per million for parent fenbendazole in liver. A marker residue concentration of 0.8 part per million in liver corresponds to a concentration for total residues of fenbendazole of 10 parts per million in liver. The safe concentrations² for total residues of fenbendazole in the uncooked edible tissues of cattle are 5 parts per million in muscle, 10 parts per million in liver, 15 parts per million in kidney, and 20 parts per million in fat.

(b) *Swine*. A tolerance¹ for marker residues of fenbendazole in swine is not needed. The safe concentrations² for the total residues of fenbendazole in the uncooked edible tissues of swine are 5 parts per million in muscle, 15 parts per million in liver, 20 parts per million in kidney, and 20 parts per million in skin and fat.

¹ As used in this section: "Tolerance" refers to a concentration of a marker residue in the target tissue selected to monitor for total residues of the drug in the target animal.

² "Safe concentrations" refer to the concentrations of total residues considered safe in edible tissues.

[49 FR 3846, Jan. 31, 1984]

§ 556.277 Fenprostalene.

A tolerance for marker residue of fenprostalene in cattle is not needed. The safe concentrations for the total residues of fenprostalene in the uncooked edible tissues of cattle are 10 parts per billion in muscle, 20 parts per billion in liver, 30 parts per billion in kidney, 40 parts per billion in fat, and 100 parts per billion in the injection site. As used in this section "tolerance" refers to a concentration of a marker residue in the target tissue selected to monitor for total residues of the drug in the target animal, and "safe concentrations" refer to the concentrations of total residues considered safe in edible tissues.

[49 FR 26716, June 29, 1984]

§ 556.290 Furazolidone.

A tolerance of zero is established for residues of furazolidone in the uncooked edible tissues of swine.

§ 556.300 Gentamicin sulfate.

(a) A tolerance of 0.1 part per million is established for negligible residues of gentamicin sulfate in the uncooked edible tissues of turkeys.

(b) Tolerances are established for total residues of gentamicin in edible tissues of swine as follows: 0.1 part per million in muscle, 0.3 part per million in liver, and 0.4 part per million in fat and kidney. A microbiological determinative procedure and an HPLC confirmatory procedure for gentamicin have been developed to assay gentamicin in kidney at 0.4 ppm. Since residues of gentamicin as the parent compound and total residues are equal, the marker (parent drug) residue concentration of 0.4 ppm in kidney corresponds to 0.4 ppm of total residue.

[48 FR 791, Jan. 7, 1983]

§ 556.308 Halofuginone hydrobromide.

The marker residue selected to monitor for total residues of halofuginone in broilers is parent halofuginone and the target tissue selected is liver. A tolerance is established in broilers of 0.1 part per million for parent halofuginone in liver. A marker residue concen-

tration of 0.1 part per million in liver corresponds to a concentration for total residues of halofuginone of 0.3 part per million in liver. The safe concentrations for total residues of halofuginone in the uncooked edible tissues of broilers are 0.1 part per million in muscle, 0.3 part per million in liver, and 0.2 part per million in skin with adhering fat. As used in this section, "tolerance" refers to a concentration of a marker residue in the target tissue selected to monitor for total residues of the drug in the target animal, and "safe concentrations" refers to the concentrations of total residues considered safe in edible tissues.

[50 FR 33718, Aug. 21, 1985]

§ 556.310 Haloxon.

A tolerance of 0.1 part per million is established for negligible residues of haloxon (3-chloro-7-hydroxy-4-methylcoumarin bis(2-chloroethyl) phosphate) in the edible tissues of cattle.

[40 FR 13942, Mar. 27, 1975, as amended at 45 FR 10333, Feb. 15, 1980]

§ 556.320 Hydrocortisone.

A tolerance is established for negligible residues of hydrocortisone (as hydrocortisone sodium succinate or hydrocortisone acetate) in milk at 10 parts per billion.

§ 556.330 Hygromycin B.

A tolerance of zero is established for residues of hygromycin B in or on eggs and the uncooked edible tissues of swine and poultry.

§ 556.344 Ivermectin.

The marker residue tolerance and safe concentrations for total residues in edible tissues of target animals are as follows:

(a) *Cattle and reindeer.* The marker residue used to monitor the total residues of ivermectin in cattle and reindeer is 22,23-dihydro-avermectin B_{1a}. The target tissue selected in liver. A tolerance is established for 22, 23-dihydro-avermectin B_{1a} in cattle and reindeer of 15 parts per billion in liver. A marker residue concentration of 15 parts per billion in liver corresponds to a concentration for total residues of ivermectin of 50 parts per billion in

liver. The safe concentrations for total residues of ivermectin in uncooked edible tissues of cattle and reindeer are 25 parts per billion in muscle, 50 parts per billion in liver, 75 parts per billion in kidney, and 100 parts per billion in fat.

(b) *Swine.* The marker residue used to monitor the total residues of ivermectin in swine 22,23-dihydro-avermectin B_{1a}. The target tissue selected is liver. A tolerance is established for 22,23-dihydro-avermectin B_{1a} in swine of 20 parts per billion in liver. A marker residue concentration of 20 parts per billion in liver corresponds to a concentration for total residues of ivermectin of 75 parts per billion in liver. The safe concentrations for total residues of ivermectin in uncooked edible tissues of swine are 25 parts per billion in muscle, 75 parts per billion in liver, 100 parts per billion in kidney, and 100 parts per billion in fat.

(c) *Sheep.* The marker residue used to monitor the total residues of ivermectin in sheep is 22,23-dihydro-avermectin B_{1a} (H₂B_{1a}). The target tissue selected is liver. A tolerance is established for H₂B_{1a} in sheep of 30 parts per billion in liver. A marker residue concentration of 30 parts per billion in liver corresponds to a concentration for total residues of ivermectin of 125 parts per billion in liver. The safe concentrations for total residues of ivermectin in uncooked edible tissues of sheep are 25 parts per billion in muscle and 125 parts per billion in liver, kidney, and fat.

[51 FR 27021, July 20, 1986, as amended at 53 FR 27958, July 26, 1988]

§ 556.347 Lasalocid.

As used in this section "tolerance" refers to a concentration of a marker residue in the target tissue selected to monitor for total residues of the drug in the target animal, and "safe concentrations" refers to the concentrations of total residues considered safe in edible tissues.

(a) *Chickens.* The marker residue selected to monitor for total residues of lasalocid in chickens is parent lasalocid. The target tissue is skin with adhering fat. A tolerance for the marker is established in chickens of 0.3 part

per million for parent lasalocid in skin with adhering fat. A marker residue concentration of 0.3 part per million in skin with adhering fat corresponds to a concentration for total residues of lasalocid of 7.2 parts per million in liver. The safe concentrations for total residues of lasalocid in the uncooked edible tissues of chickens are 1.2 parts per million in muscle, 2.4 parts per million in skin with adhering fat, and 7.2 parts per million in liver.

(b) *Cattle*. The marker residue selected to monitor for total residues of lasalocid sodium in cattle is parent lasalocid and the target tissue selected is the liver. A tolerance is established in cattle of 0.7 part per million for parent lasalocid in liver. A marker residue concentration of 0.7 part per million in liver corresponds to a concentration for total residues of lasalocid of 4.8 parts per million in liver. The safe concentrations for total residues of lasalocid in the uncooked edible tissues of cattle are 1.2 parts per million in muscle, 4.8 parts per million in liver and in fat, and 3.6 parts per million in kidney.

(c) *Sheep*. A tolerance for marker residues of lasalocid sodium in sheep is not needed. The safe concentrations for total residues of lasalocid in the uncooked edible tissues of sheep are 1.2 parts per million in muscle and 6 parts per million in liver, fat, and kidney.

(49 FR 27316, July 3, 1984, as amended at 49 FR 29087, July 18, 1984)

§ 556.350 Levamisole hydrochloride.

A tolerance of 0.1 part per million is established for negligible residues of levamisole hydrochloride in the edible tissues of cattle, sheep, and swine.

§ 556.360 Lincomycin.

Tolerances are established for residues of lincomycin as follows: 0.15 part per million for negligible residues in milk; and 0.1 part per million for negligible residues in the edible tissues of chickens and swine.

§ 556.375 Maduramicin ammonium.

A tolerance is established for residues of maduramicin ammonium in chickens as follows:

(a) A tolerance for maduramicin ammonium (marker residue) in chickens is 0.38 parts per million in fat (target tissue). A tolerance refers to the concentration of marker residues in the target tissue used to monitor for total drug residues in the target animals.

(b) The safe concentrations for total maduramicin ammonium residues in uncooked edible chicken tissues are: 0.24 parts per million in muscle; 0.72 parts per million in liver; 0.48 parts per million in skin; and 0.48 parts per million in fat. A safe concentration refers to the total residue concentration considered safe in edible tissues.

(54 FR 5229, Feb. 2, 1989)

§ 556.380 Melengestrol acetate.

No residues of melengestrol acetate (17-hydroxy-6-methyl-16-methylene-pregna-4,6-diene-3,20-dione acetate) may be found in uncooked edible tissues of cattle as determined by the following method of analysis:

I. *Method of analysis—melengestrol acetate*. A gas-liquid chromatographic (GLC) method for melengestrol acetate (MGA) in frozen bovine tissue is described which removes, through several partition and chromatography cleanup steps, most interfering materials before injection of the sample onto the column for detection. MGA is extracted from lean tissues with ethanol and transferred, after dilution with water, into chloroform. MGA in fatty tissues is extracted with hexane and transferred first into aqueous methanol, then into methylene chloride. The residue from either extract, after evaporation of solvent, is chromatographed on silica gel to remove lipid materials using hexane and a mixture of ethyl ether-benzene. MGA is eluted with ethyl acetate. The residue, after evaporation, is dissolved in hexane and transferred first into aqueous methanol and then into methylene chloride. The dried residue is transferred to aluminum oxide thin layer chromatography (TLC) plates which are developed in a benzene-chloroform-ethyl acetate system. The zone containing MGA is removed and eluted with ethanol. The ethanol is evaporated and the MGA is dissolved into an exact volume of chloroform. MGA is injected onto a 3-percent QF-1 column in an all-glass system and quantitated by peak height measurements from a flame ionization detector.

MGA can be detected at a level of 25 parts per billion with negligible interference from tissues or reagents. Observed recovery $\pm$ estimated standard deviation at 25 parts per

billion in muscle, liver, and fat is 74.4 ± 8.0 percent.

II. *Reagents.* All solvents must be GLC pure when processed through the entire procedure in the absence of tissue, see VII *Recovery study* below.

A. Air—20 pounds per square inch purified by passage through a Linde Molecular Sieve, type 4A, $\frac{1}{8}$ -inch pellets or equivalent.

B. Aluminum oxide GF254, Brinkman Instruments, or equivalent.

C. Benzene—Burdick and Jackson Laboratories, Distilled-in-Glass grade, or equivalent.

D. Chloroform—Burdick and Jackson Laboratories, Distilled-in-Glass grade, or equivalent.

E. Column packing—3-percent QF-1 on Gas Chrom Q, 100-120 mesh, Applied Science Laboratories, Inc., or equivalent.

F. Dry ice.

G. Ethanol—absolute, synthetic, Gold Shield, Commercial Solvents Corp., or equivalent. A 25-milliliter portion roto-evaporated to dryness, taken up in 0.1 milliliter chloroform and 10 microliters injected into the gas chromatograph should show no contaminants. Contaminated alcohol must be redistilled in an all-glass system and retested.

H. Ethanol—190 proof, synthetic, Gold Shield, Commercial Solvents Corp., or equivalent.

I. Ethyl acetate—Burdick and Jackson Laboratories, Distilled-in-Glass grade, or equivalent.

J. Ethyl ether—anhydrous, Mallinckrodt AR, 1-pound can, or equivalent.

K. Glassware cleaner—Haemo-Sol, Scientific Products, or equivalent.

L. Helium—99.5 percent minimum, The Matheson Co., or equivalent.

M. Hexane—Burdick and Jackson Laboratories, Distilled-in-Glass grade, or equivalent.

N. Hydrogen—99.5 percent minimum, Ohio Chemical Co., or equivalent.

O. Melengestrol acetate—MGA Standard, 99.5 percent purity, The Upjohn Co.

P. Methanol—Burdick and Jackson Laboratories, Distilled-in-Glass grade, or equivalent.

Q. Methylene chloride—Burdick and Jackson Laboratories, Distilled-in-Glass grade, or equivalent.

R. Nitrogen—filtered, see III-D below, The Matheson Co., or equivalent.

S. Progesterone—The Upjohn Co., or equivalent.

T. Silica gel—for chromatographic columns, 50-200 mesh, G. Frederick Smith Chemical Co., or equivalent.

U. Sodium sulfate—anhydrous, Mallinckrodt AR, granular, or equivalent.

V. Water—double distilled in glass or deionized.

W. Solvent mixtures—ratios by volume:
1. 10:1:1 benzene-chloroform-ethyl acetate.

2. 1:1 chloroform-methanol.

3. 19:1 ethanol, absolute-double distilled water.

4. 1:19 ethyl ether-benzene.

5. Hexane saturated with 7:3 methanol-water.

6. 7:3 methanol-water.

7. 9:1 methanol-water.

8. Saturated sodium sulfate solution, aqueous.

III. *Special apparatus.* A. Adapters—40, No. 5225, Ace Glass, Inc., or equivalent.

B. Blender—Waring Blender, or equivalent.

C. Chromatography columns—glass columns 28 (inside diameter) $\times$ 600 millimeters, fitted with Teflon stopcocks and medium porosity, sintered glass disks, Fisher and Porter 274-100, or equivalent.

D. Filters—Koby "Junior," air purifier and flow equalizer, low pressure, The Koby Corp., or equivalent.

E. Filtrator—Fisher Filtrator, Fisher Scientific Co., or equivalent.

F. Gas chromatograph—Micro Tek 230, or F and M 402, or equivalent. Instrument must have an all-glass on-column injection system and a flame detector. Electrometer sensitivity of 10^{-12} amperes and recorder sensitivity of 1 millivolt.

G. Gas chromatography columns—unborosilicate glass tubing, 0.2362 ± 0.013 inch outside diameter and 0.118 ± 0.01 inch inside diameter, Wilkens Anderson Co., or equivalent. Bend 2-foot and 3-foot pieces of tubing into the proper design for the instrument to be used. Pack the columns with 16 and 31 inches, respectively, of 3-percent QF-1 and plug both ends with 0.5 centimeter of loosely packed, silanized glass wool. Pack far enough from the ends so that no part of the column packing or glass wool will be inside the heated injection port or outlet fitting. Insert column into the GLC oven and condition with carrier gas off for 2 hours at 200 C., then at 220° C. overnight with the carrier gas on at a rate of 10 milliliters per minute.

H. Micropipettes—5 and 25 microliters, Microcap Disposable Pipettes, Drummond Scientific Co., or equivalent.

I. Micropipette—500 microliters, E14 type, Microchemical Specialties Co., or equivalent.

J. Miniature jet evaporator—several transfer pipettes (see III-L below) connected through a manifold to a nitrogen supply.

K. Oven—110° C.

L. Pipettes—transfer pipettes, 9-inch disposable pipettes, Scientific Products, or equivalent.

M. Roto-evaporator—four to six small Renco evaporators, or equivalent, controlled

with 4-millimeter bore stopcocks connected to a manifold which leads to two condensation traps (1-2 liters) connected in series to a vacuum pump of 140 liters per minute free air capacity. The traps are cooled with a dry ice-solvent mixture. The time for roto-evaporation of 200 milliliters of 7:3 methanol-water is 35-40 minutes. Each sample in a round-bottomed flask is connected with two adapters (see III-A above) in a series to an evaporator and heated in a thermostatically controlled water bath at 45° C.

N. Separatory funnels—fitted with Teflon stopcocks, 125, 500, and 2,000 milliliters.

O. Shevsky-Stafford tubes—6.5 milliliters, Arthur H. Thomas Co., or equivalent. Must be calibrated at the 0.100 milliliter mark to contain 0.100 ± 0.002 milliliters.

P. Silanized glass wool—Applied Science laboratories, or equivalent.

Q. Sintered glass Buchner funnels—fine porosity 2.5 x 5.0 centimeters.

R. Syringe—25-Microliter, Hamilton No. 802, Hamilton Co., Inc., or equivalent.

S. Thin layer chromatography equipment—spreader suitable for preparing five plates, 0.75-millimeter thickness. Glass tanks for developing TLC plates.

T. TLC plates—200 x 200 millimeters, prepared as follows:

1. Place 5 plates (200 x 200 millimeters) in the template, wipe the surface with absolute ethyl alcohol and dry with lintless tissue.

a. TLC plates are best cleaned by immersion in a sonic-oscillation bath.

b. Hand washing is not recommended unless absolutely necessary.

2. Adjust the spreader for 0.75 millimeters.

3. Weigh out 90 grams of aluminum oxide and place in a clean, dry blender jar.

a. Add 140 milliliters of distilled water and blend at low speed for 30 seconds.

b. Remove the jar from the blender and swirl the contents.

c. After 90 seconds has elapsed from the time the blender was turned on, pour the slurry into the spreader and coat the five plates.

d. It may be necessary to make minor operational changes such as amount of water and mixing time in order to obtain plates of uniform thickness free of checks and bubbles.

i. If checks or cracks appear, decrease the amount of water.

ii. If bubbles appear, decrease blending time or speed.

4. Allow the plates to dry 2 days or longer at room temperature.

a. Plates aged 2 to 4 weeks show less tendency to flake in the mobile solvent systems.

b. Plates may be stored on the bench exposed to laboratory air if it can be demonstrated that no air contaminants are present

as shown by a TLC blank run through the GLC starting with procedure step V-G9.

5. Activate the plates for 1 hour at 110° C. in a hot air oven, cool 30 minutes in laboratory air.

a. Use plates the same day they are activated.

b. Oven should be free of contaminants that may be absorbed by the plates as shown by a TLC blank run through the GLC starting with procedure step V-G9.

c. Relative humidity of 40-60 percent aids in dissipating the static charge which appears to be characteristic of heated alumina plates. Unless this charge is dissipated, attraction of alumina for the spotting pipette causes disruption of the surface.

d. If humidity conditions cannot be met, longer standing will suffice to dissipate the charge.

6. Scribe the TLC plates at right angles to the direction in which they are poured in the following manner:

a. Remove 2 millimeters alumina from vertical edges of each plate.

b. Scribe the rest of the plate with 2-millimeter wide lines so as to give two 80-millimeter strips and one 20-millimeter vertical strip between them.

U. Tissue homogenizer—Lourdes tissue homogenizer with 300-milliliter stainless steel cups fitted with silicone rubber gaskets. Do not use any lubricant. Reduce wear between cup head and shaft bushings with Teflon-fiberglass washers made from Teflon tape impregnated with 15 percent glass, 0.015 inch thick, Detroit Ball Bearing Co., or equivalent.

V. Ultraviolet lamp—Mineralight Model 2L-2537 (shortwave), or equivalent.

W. Vacuum oven—20-35° C., 20-30 millimeters mercury.

X. Volumetric flasks—1 milliliter.

Y. Vortex mixer—Fisher Mini-Shaker, or equivalent.

IV. *Standard solutions.* A. Stock solution A—6.00 milligrams of MGA in 100 milliliters of absolute ethanol.

B. Stock solution B—dilute 5 milliliters of stock solution A to 200 milliliters with absolute ethanol.

C. Stock solution C—20 milligrams of MGA in 100 milliliters of absolute ethanol.

D. Stock solution D—Dilute 5 milliliters stock solution C to 100 milliliters with chloroform.

E. Stock solution E—10 milligrams of MGA and 10 milligrams of progesterone in 10 milliliters of absolute ethanol.

F. Stock solution F—10 milligrams of MGA in 10 milliliters of absolute ethanol.

V. *Procedure.* A. Preparation of glassware. All glassware should be washed in detergent to remove contaminants and rinsed in water to remove traces of cleaning agent. Rinse with solvents before using.

B. Preparation of sample:

1. Grind the fresh tissue in a meat grinder and store in a suitable container in a deep freeze.

2. Chill the leg bones in the refrigerator for 24 hours, saw them lengthwise (commercial meat bandsaw), remove the bone marrow, and place in the deep freeze.

3. Steam the tripe for 5 minutes and strip off the muscle layer and store in deep freeze.

C. Extraction procedure for muscle, liver, kidney, and tripe:

1. Clean homogenizer by disassembling mixer heads completely and soaking in detergent with the cups. Keep all parts from each mixer head separated from those of the other assemblies. Brush all parts and rinse thoroughly with tap water and then with distilled water. Let dry and reassemble the mixer heads without using a lubricant.

2. Weigh 60 grams of the partially thawed tissue into a 300-milliliter homogenizing cup and refreeze the unused portion immediately.

3. Add 175 milliliters of 190 proof ethanol and a circle of Whatman filter paper No. 40, 12.5 centimeters, as a filter aid.

4. Homogenize for 2 minutes in an ice bath.

5. Filter the slurry through Whatman filter paper No. 40, 12.5 centimeters, in a Buchner funnel into a 1-liter filter flask using a vacuum supply.

6. Wash the cut with 20-25 milliliters of 190 proof ethanol using a wash bottle and filter the washings through the Buchner funnel.

7. Transfer the dry filter cake with its filter paper to the cup and add 175 milliliters of 190 proof ethanol.

8. Homogenize for 2 minutes and filter the slurry.

9. Repeat step 7, but this time homogenize the dry cake without its filter paper for 2 minutes and filter.

10. Mark the level of the combined alcohol eluates in the 1-liter filter flask and quantitatively transfer it to a 2-liter separatory funnel.

11. Add water to the marked level; add 100 milliliters of water and 20 milliliters of saturated sodium sulfate solution to the flask, mix, and transfer the mixture to the separatory funnel.

12. Add 100 milliliters of chloroform and shake the separatory funnel vigorously for 1 minute.

13. Let stand for 30 minutes or until complete phase separation takes place. If the chloroform layer is less than 50 milliliters, add 25 milliliters more of chloroform and shake again.

14. Drain the chloroform phase into a 1-liter round-bottomed flask.

15. Repeat procedure steps V-12, 13, and 14 three more times.

16. Roto-evaporate the combined chloroform extracts and remove the last trace of water in the following manner avoiding violent bubbling during roto-evaporation.

a. This can be done by restricting the vacuum supply by partially opening the stopcock slowly or by starting the roto-evaporator with the round-bottomed flask just out of the water bath. When flask is cool or shows frosting, place it into water bath.

b. To the flask add with swirling 25 milliliters of hexane followed by 25 milliliters of absolute ethanol.

c. Swirl until the solids and/or oil are dissolved or suspended in the solvents and roto-evaporate.

d. Add 25 milliliters of absolute ethanol and roto-evaporate until 15 minutes after the solvent has been removed.

17. Close the stopcock and open the system at the glass joint between the adapters.

a. This prevents back-flushing of contaminants from the roto-evaporator.

b. *Stopping place.* Leave the adapter in place, stopper, and store in refrigerator or deep freeze.

c. Storage of sample in the solvent should be avoided.

D. Extraction procedure for fat and bone marrow:

1. Clean homogenizer cups and heads, procedure step V-C1; weigh samples as in procedure step V-C2.

2. Add 150 milliliters of hexane and warm on a steam bath without boiling.

3. Stir the solution with a spatula until the fat dissolves.

4. Filter the warm solution through Whatman No. 40 filter paper, 12.5 centimeters, into a 1-liter filter flask.

5. Transfer the filter cake, including filter paper, to the cup and add 150 milliliters of hexane.

6. Homogenize for 2 minutes in an ice bath, rewarm the cup, and filter the warm solution into the filter flask.

7. Repeat the homogenization and extraction of the filter cake one more time.

8. Warm the filter flask until the solution is relatively clear and transfer the warm hexane solution into a 2-liter separatory funnel.

9. Add 500 milliliters of hexane, 250 milliliters of 9:1 methanol-water, and shake vigorously for 1 minute.

10. Let stand 30 minutes and drain the lower phase into a 2-liter separatory funnel.

11. Extract with three 250-milliliter portions of 9:1 methanol-water and combine the extracts.

12. To the combined filtrates in the 2-liter separatory funnel, add 500 milliliters of water and 2 milliliters of saturated sodium sulfate solution to give 55 to 60 percent aqueous methanol.

13. Shake vigorously for 1 minute the aqueous methanol with 300 milliliters of methylene chloride. If the phases do not separate well, add 2 milliliters of saturated sodium sulfate solution and shake again.
14. Let phases stand 20 minutes and drain into a 1-liter round-bottomed flask.
15. Extract with three successive portions of 100 milliliters of methylene chloride.
16. Roto-evaporate the combined extracts as in procedure step V-C16.
17. *Stopping place.* Leave adapter in place, stopper, and store in the refrigerator or deep freeze.
- E. Defatting on silica gel columns: 1. Prepare silica gel column as follows:
 - a. Clean the column with 50 milliliters of absolute ethanol, allowing it to flow through the sintered disk. Aspirate air through the column until dry.
 - b. Half fill a column with hexane, slurry 20 grams silica gel in hexane, and pour it into the column.
 - c. Rinse the sides of the beaker and column with hexane.
 - d. Adjust the flow rate to 8-10 milliliters per minute.
 - e. While maintaining at least 15 centimeters of solvent, slowly add anhydrous sodium sulfate to a depth of 3 centimeters. The sodium sulfate layer should be free of air bubbles and should not disrupt the silica gel surface.
2. Take residue from procedure steps V-C17b and V-D17. Remove and rinse adapter with stopper in place as follows:
 - a. Invert and pour 20 milliliters of hexane into the adapter and swirl.
 - b. Pour the contents onto the residue.
 - c. Rinse the adapter twice with hexane using a wash bottle and transfer the washings to the residue.
3. Swirl and transfer the hexane solution to the silica gel column.
4. Allow the solution to be completely absorbed into the column, but do not allow the column to go to dryness.
5. Maintain a flow rate of 8-10 milliliters per minute.
6. Rinse the round-bottomed flask twice with 10-milliliter portions of hexane and transfer to the column.
7. Wash the column with the following solvents, discarding the effluents:
 - a. Rinse the round-bottomed flask with 75 milliliters of hexane and pour onto the column.
 - b. 350 milliliters of 1:19 ethyl ether-benzene (prepared daily from fresh ether, do not reuse opened cans).
8. Elute MGA fraction with 350 milliliters of ethyl acetate into a 1-liter round-bottomed flask and roto-evaporate off the solvent.
 - a. Discard the adapters.
 - b. *Stopping place.* Stopper and store in refrigerator or deep freeze.
- F. Solvent partition: 1. Transfer the residue to a 125-milliliter separatory funnel using two 20-milliliter portions of hexane saturated with 7:3 methanol-water.
2. Extract the hexane phase with 40 milliliters of 7:3 methanol-water, first rinsing the round-bottomed flask with the aqueous methanol.
 - a. Shake the funnel vigorously for 1 minute; let the phases separate at least 1 hour.
 - b. Drain the lower phases into a 500-milliliter separatory funnel containing 50 milliliters of methylene chloride, 80 milliliters of water, and 0.5 milliliter of saturated sodium sulfate solution.
3. Repeat step 2 four more times combining all extracts in the 500-milliliter separatory funnel.
4. Stopper the 500-milliliter separatory funnel, invert carefully, and vent immediately. Shake the funnel cautiously, venting frequently. When all pressure subsides, shake the funnel vigorously for 1 minute, wait 20-30 minutes, and drain the lower phase into a 500-milliliter round-bottomed flask. This precaution does not apply to the subsequent shakings.
5. Extract with three more 50-milliliter portions of methylene chloride, each time draining the lower phase into the flask.
6. Roto-evaporate the combined extracts until all the solvent has been removed. *Stopping place.* Stopper and store in refrigerator or deep freeze.
- G. Thin layer chromatography. 1. Transfer the residue to a 1-milliliter volumetric flask using five 2-milliliter portions of 1:1 chloroform-methanol.
 - a. A 1-milliliter volumetric flask holds over 2 milliliters.
 - b. After each transfer, place the 1-milliliter flask in a water bath at 35-40° C. and evaporate the solvents on the miniature jet evaporator, see apparatus III-J.
 - c. Evaporate the last portion under nitrogen to just below the 1-milliliter mark.
 - d. Label this flask "A".
 - e. Bring the volume back to the 1-milliliter mark, stopper, and mix.
2. Accurately transfer 500 microliters from flask "A" into another 1-milliliter volumetric flask and evaporate to dryness under nitrogen.
 - a. Label this flask "B".
 - b. This will ultimately be the portion of the split sample that is assayed by GLC.
3. Add 25 microliters of stock solution F to volumetric flask "A" and evaporate the solvents under nitrogen.
 - a. This half will be used to locate the MGA area on the plate.
 - b. All samples are split and fortified as described above in procedure steps V-G2 and V-G3.

- c. *Stopping place.* Stopper and store in refrigerator or deep freeze.
 4. To the residue in flasks "A" and "B", add 10-12 drops of 1:1 chloroform-methanol.
 5. Apply the entire sample in flask "A" across the entire 80-millimeter band 3 centimeters from the bottom of the plate.
 - a. Apply the sample in 10- to 20-microliter portions using a 25-microliter pipette. Apply the residue as a band 10 to 15 millimeters wide and 80 millimeters long. Flow the solution onto the plate as rapidly as possible with no forced drying.
 - b. Label this side of the plate "A".
 6. Rinse the flask with 10 drops of 1:1 chloroform-methanol and apply to the same streaked area as soon as possible.
 7. Repeat once more with 5 drops.
 8. Place sample "B" on the other 80-millimeter strip in a similar manner as in procedure step V-G 5, 6, and 7, and label this side of the plate "B".
 9. Spot 5 microliters of stock solution E on the 20-millimeter strip.
 10. Allow the plate to dry for 15 minutes at room temperature.
 11. Place the plate in a tank containing fresh 1:1 chloroform-methanol. Saturation of tank atmosphere is not necessary.
 12. Remove the plate from the tank when the solvent front has moved 5 centimeters from the bottom of the plate. MGA and similar substances concentrate as a narrow band at the solvent front.
 13. Remove and air dry the plate in a horizontal position on a cork ring for all subsequent plate-drying steps.
 14. Dry for 15 minutes at room temperature and for another 15 minutes in a vacuum oven.
 15. Place the plate in a tank containing fresh 10:1:1 benzene-chloroform-ethyl acetate. Saturation of tank atmosphere is unnecessary.
 16. Allow the solvent to rise 17 centimeters from the bottom of the plate.
 17. Determine the position of MGA on the plate in section A with UV radiation referring to the lower spot in the center section. MGA will be below progesterone.
 18. Scribe horizontal lines on section B above and below the MGA area using section A as a guide to determine the width of the band to be removed. Do not disturb section A.
 19. Wash a sintered glass funnel with chloroform, hexane, and alcohol using a vacuum supply.
 20. Scrape the MGA zone with a clean razor blade onto a piece of weighing paper and transfer the scrapings to the sintered glass funnel.
 - a. Do not rinse the weighing paper with alcohol.
 - b. Clean razor blade with hexane before and after each sample.
 21. Add four 5-milliliter portions of 1:1 ethanol-water, stir with a glass rod, let stand 5 minutes, and filter with vacuum into a 50-milliliter round-bottomed flask using a filtrator.
 22. Roto-evaporate the combined filtrate. *Stopping place.* Stopper and store in a refrigerator or deep freeze.
- H. Gas liquid chromatography:
1. Transfer the residue from the round-bottomed flask to a Shievy-Stafford tube with four 1-milliliter portions of chloroform.
 2. Place the tubes into a water bath (36-40° C.) and evaporate the solvent with a gentle stream of nitrogen, using the minute jet evaporator.
 3. Rinse the sides down with approximately 1 milliliter of chloroform and once again evaporate the solvent.
 4. Remove the tube from the evaporator as soon as possible after solvent has been removed.
 5. Bring the volume up to the 0.1 milliliter mark with chloroform and swirl with a vortex mixer.
 6. On a 2-foot conditioned column, adjust the gas flow and oven temperature to give a 10-15 minute retention time and adjust attenuation to give a peak height of 20-35 millimeters for 0.1 micrograms of MGA.
 - a. Suggested parameters are: Oven temperature, 210°-225° C.; detector temperature, 275°-280° C.; inlet temperature, 250° C.; carrier gas flow for helium, 60-120 milliliters per minute, for hydrogen, 40-60 milliliters per minute, for air, 300 milliliters per minute; chart speed, 0.25-0.5 inch per minute.
 - b. Do not exceed an oven temperature of 230° C.
 7. Inject 10 microliters of stock solution D and measure the peak height in millimeters.
 8. Inject 10 microliters of the sample and measure the peak height in millimeters.
 9. For fat samples or problem samples use the 3-foot column providing a longer retention time of 16-20 minutes.
- VI. *Calculations.* Calculate the parts per billion MGA by the following formula:
- $$\text{Parts per billion} = \frac{\text{Peak height of unknown}}{\text{Peak height of standard}} \times 33.3$$
- VII. *Recovery study.* A. Fortification of reagent blank:
1. For those using this method for the first time either for recovery study or tissue assay, a solvent blank and solvent fortified with MGA should be processed through the entire procedure. This preliminary operation will establish whether or not the procedure is free from contamination arising from solvents and glassware and demonstrate the level of recovery of standard MGA. Level of recovery should be in the same range as the samples.

2. Place 175 milliliters of 190 proof ethanol into the homogenizer.

3. To another 175 milliliters of 190 proof ethanol in a homogenizer cup add 1 milliliter of stock solution B.

4. Assay both samples as described in the procedure beginning with the extraction step V-C4.

B. Fortification of the samples:

1. Weigh 60-gram portions of the unfortified tissue into homogenizer cups and set half of them aside to serve as tissue blanks.

2. Add to the remaining samples 1 milliliter of stock solution B to serve as fortified samples to which 25 parts per billion have been added.

3. Assay both fortified and unfortified tissue as described in the procedure section beginning with the extraction step V-C3 or the extraction step V-D2, whichever is appropriate.

§ 556.390 Methylparaben.

A tolerance of zero is established for residues of methylparaben in milk from dairy animals.

§ 556.400 Methylprednisolone.

A tolerance is established for negligible residues of methylprednisolone in milk at 10 parts per billion.

§ 556.410 Metoserbate hydrochloride.

A tolerance of 0.02 part per million is established for negligible residues of metoserbate hydrochloride (methyl- α -methyl-18-epireserbate hydrochloride) in uncooked edible tissues of chickens.

§ 556.420 Monensin.

(a) *Cattle*. A tolerance of 0.05 part per million is established for negligible residues of monensin in the edible tissues of cattle.

(b) *Chickens, turkeys, and quail*. A tolerance for marker residues of monensin in chickens, turkeys, and quail is not needed. The safe concentrations for total residues of monensin in chickens, turkeys, and quail are 1.5 parts per million in muscle, 3.0 parts per million in skin with adhering fat, and 4.5 parts per million in liver. "Tolerance" in this paragraph refers to the concentration of a marker residue in the target tissue selected to monitor total residues of the drug in the target animals. "Safe concentrations" refers to the concentration of total residues considered safe in edible tissues.

[50 FR 32394, Aug. 12, 1985, as amended at 52 FR 15718, Apr. 30, 1987; 53 FR 40060, Oct. 13, 1988]

§ 556.425 Morantel tartrate.

The marker residue selected to monitor for total residues of morantel tartrate in cattle is *N*-methyl-1,3-propanediamine (MAPA). The target tissue selected is liver. Residue concentrations are determined by measuring the morantel residues convertible to MAPA. A tolerance for MAPA is established in cattle of 0.70 part per million in liver. A marker residue concentration of 0.70 part per million in liver corresponds to a concentration for total residues of morantel tartrate of 2.40 parts per million in liver. The safe concentrations for total residues of morantel tartrate in the uncooked edible tissues of cattle are 1.20 parts per million in muscle, 2.40 parts per million in liver, 3.60 parts per million in kidney, and 4.80 parts per million in fat. A tolerance for the marker residue of morantel tartrate in milk is not needed. The safe concentration for total residues of morantel tartrate in milk is 0.40 part per million. "Tolerance" in this section refers to a concentration of a marker residue selected to monitor for total residues of the drug in the target animal. "Safe concentrations" refer to the concentrations of total residues considered safe in edible tissues and milk.

[51 FR 9005, Mar. 17, 1986]

§ 556.428 Narasin.

A tolerance for narasin residues in chickens is not needed. The safe concentrations for total narasin residues in uncooked edible chicken tissues are: 0.6 part per million in muscle; 1.8 parts per million in liver; 1.2 parts per million in skin with adhering fat and fat. A tolerance refers to the concentration of marker residues in the target tissue used to monitor for total drug residues in the target animals. A safe concentration refers to the total residue concentration considered safe in edible tissues.

[51 FR 29097, Aug. 14, 1986]

§ 556.430

§ 556.430 Neomycin.

Tolerances are established for residues of neomycin in food as follows: 0.25 part per million (negligible residue) in edible tissues of calves; and 0.15 part per million (negligible residue) in milk.

§ 556.440 Nequinat.

A tolerance of 0.1 part per million is established for negligible residues of nequinat in the uncooked edible tissues of chickens.

§ 556.445 Nicarbazin.

A tolerance of 4 parts per million is established for residues of nicarbazin in uncooked chicken muscle, liver, skin, and kidney.

[42 FR 56729, Oct. 28, 1977]

§ 556.460 Novobiocin.

Tolerances for residues of novobiocin are established at 0.1 part per million in milk from dairy animals and 1 part per million in the uncooked edible tissues of cattle, chickens, turkeys, and ducks.

[47 FR 18590, Apr. 30, 1982]

§ 556.470 Nystatin.

A tolerance of zero is established for residues of nystatin in or on eggs and the uncooked edible tissues of swine and poultry.

§ 556.480 Oleandomycin.

Tolerances are established for negligible residues of oleandomycin in uncooked edible tissues of chickens, turkeys, and swine at 0.15 part per million.

§ 556.490 Ormetoprim.

A tolerance of 0.1 part per million is established for negligible residues of ormetoprim in the edible tissues of chickens, turkeys, ducks, salmonids, and catfish.

[51 FR 18884, May 23, 1986]

§ 556.500 Oxytetracycline.

Tolerances are established for residues of oxytetracycline in food as follows:

(a) In edible tissues of chickens and turkeys:

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(1) 3 parts per million in uncooked kidney.

(2) 1 part per million in uncooked muscle, liver, fat, and skin.

(b) 0.1 part per million in uncooked edible tissues of swine.

(c) 0.1 part per million in uncooked edible tissues of cattle, beef calves, nonlactating dairy cattle and dairy calves.

(d) A tolerance of 0.1 part per million is established for negligible residues of oxytetracycline in uncooked edible tissues of salmonids, catfish, and lobsters.

[40 FR 13942, Mar. 27, 1975, as amended at 52 FR 24293, June 30, 1987]

§ 556.510 Penicillin.

Tolerances are established for residues of penicillin and the salts of penicillin in food as follows:

(a) 0.05 part per million (negligible residue) in the uncooked edible tissues of cattle.

(b) Zero in the uncooked edible tissues of chickens, pheasants, quail, swine, and sheep; in eggs; and in milk or in any processed food in which such milk has been used.

(c) 0.01 part per million in the uncooked edible tissues of turkeys.

[40 FR 13942, Mar. 27, 1975, as amended at 43 FR 32749, July 28, 1978]

§ 556.520 Prednisolone.

A tolerance of zero is established for residues of prednisolone in milk from dairy animals.

§ 556.530 Prednisone.

A tolerance of zero is established for residues of prednisone in milk from dairy animals.

§ 556.540 Progesterone.

No residues of progesterone are permitted in excess of the following increments above the concentrations of progesterone naturally present in untreated animals:

(a) In uncooked edible tissues of steers and calves:

(1) 3 parts per billion for muscle.

(2) 12 parts per billion for fat.

(3) 9 parts per billion for kidney.

(4) 6 parts per billion for liver.

(b) In uncooked edible tissues of lambs:

(1) 3 parts per billion for muscle.

(2) 15 parts per billion for fat, kidney, and liver.

[49 FR 13873, Apr. 9, 1984]

§ 556.550 Propylparaben.

A tolerance of zero is established for residues of propylparaben in milk from dairy animals.

§ 556.560 Pyrantel tartrate.

Tolerances are established for residues of pyrantel tartrate in edible tissues of swine as follows:

(a) 10 parts per million in liver and kidney.

(b) 1 part per million in muscle.

§ 556.580 Robenidine hydrochloride.

Tolerances are established for residues of robenidine hydrochloride in edible tissues of chickens as follows:

(a) 0.2 part per million in skin and fat.

(b) 0.1 part per million (negligible residue) in edible tissues other than skin and fat.

§ 556.590 Salicylic acid.

A tolerance of zero is established for residues of salicylic acid in milk from dairy animals.

§ 556.600 Spectinomycin.

A tolerance of 0.1 part per million is established for negligible residues of spectinomycin in the uncooked edible tissues of chickens.

§ 556.610 Streptomycin.

A tolerance of zero is established for residues of streptomycin in the uncooked edible tissues of chickens, turkeys, and swine, and in eggs.

§ 556.620 Sulfabromomethazine sodium.

Tolerances for residues of sulfabromomethazine sodium in food are established as follows:

(a) In the uncooked edible tissues of cattle at 0.1 part per million (negligible residue).

(b) In milk at 0.01 part per million (negligible residue).

[47 FR 30244, July 13, 1982]

§ 556.625 Sodium sulfachloropyrazine monohydrate.

A tolerance of zero is established for residues of sodium sulfachloropyrazine monohydrate in the uncooked edible tissues of chickens.

§ 556.630 Sulfachlorpyridazine.

A tolerance of 0.1 part per million is established for negligible residues of sulfachlorpyridazine in uncooked edible tissues of calves and swine.

§ 556.640 Sulfadimethoxine.

Tolerances are established for residues of sulfadimethoxine in edible products of animals as follows:

(a) In the uncooked edible tissues of chickens, turkeys, cattle, ducks, salmonids, and catfish at 0.1 part per million (negligible residue).

(b) In milk at 0.01 part per million (negligible residue).

[40 FR 13942, Mar. 27, 1975, as amended at 49 FR 46371, Nov. 26, 1984; 51 FR 18884, May 23, 1986]

§ 556.650 Sulfaethoxypyridazine.

Tolerances for residues of sulfaethoxypyridazine in food are established as follows:

(a) Zero in the uncooked edible tissues of swine and in milk.

(b) 0.1 part per million (negligible residue) in uncooked edible tissues of cattle.

§ 556.660 Sulfamerazine.

A tolerance of zero is established for residues of sulfamerazine (N'-[4-methyl-2-pyrimidinyl]sulfanilamide) in the uncooked edible tissues of trout.

§ 556.670 Sulfamethazine.

A tolerance of 0.1 part per million is established for negligible residues of sulfamethazine in the uncooked edible tissues of chickens, turkeys, cattle, and swine.

[47 FR 25323, June 11, 1982]

§ 556.680 Sulfanitran.

A tolerance of zero is established for residues of sulfanitran (acetyl(p-nitrophenyl) sulfanilamide) and its metabolites in the uncooked edible tissues of chickens.

§ 556.690

§ 556.690 Sulfathiazole.

A tolerance of 0.1 part per million is established for negligible residues of sulfathiazole in the uncooked edible tissues of swine.

§ 556.700 Sulfomyxin.

A tolerance of zero is established for residues of sulfomyxin (N-sulfomethyl-polymyxin B sodium salt) in uncooked edible tissues from chickens and turkeys.

§ 556.710 Testosterone propionate.

No residues of testosterone, resulting from the use of testosterone propionate, are permitted in excess of the following increments above the concentrations of testosterone naturally present in untreated animals:

- (a) In uncooked edible tissues of heifers:
 - (1) 0.64 part per billion in muscle.
 - (2) 2.6 parts per billion in fat.
 - (3) 1.9 parts per billion in kidney.
 - (4) 1.3 parts per billion in liver.
- (b) [Reserved]

[52 FR 27683, July 23, 1987]

§ 556.720 Tetracycline.

A tolerance of 0.25 part per million is established for negligible residues of tetracycline in uncooked edible tissues of calves, swine, sheep, chickens, and turkeys.

§ 556.730 Thiabendazole.

Tolerances are established at 0.1 part per million for negligible residues of thiabendazole in uncooked edible tissues of cattle, goats, sheep, pheasants, and swine, and at 0.05 part per million for negligible residues in milk.

[40 FR 13942, Mar. 27, 1975, as amended at 49 FR 29958, July 25, 1984]

§ 556.738 Tiamulin.

The marker residue selected to monitor for total residues of tiamulin in swine is 8- α -hydroxymutillin and the target tissue selected is liver. A tolerance is established in swine at 0.4 part per million for 8- α -hydroxymutillin in liver. A marker residue concentration of 0.4 part per million in liver corresponds to a concentration for total residues of tiamulin of 10.8 parts per million in liver. The safe con-

centrations for total residues of tiamulin in the uncooked edible tissues of swine are 3.6 parts per million in muscle, 10.8 parts per million in liver, and 14.4 parts per million in kidney and fat.

[48 FR 41385, Sept. 15, 1983]

§ 556.739 Trenbolone.

A tolerance for total trenbolone residues in uncooked edible tissues of cattle is not needed. The safe concentration for total trenbolone residues in uncooked edible tissues of cattle is 10 parts per billion (ppb) in muscle, 100 ppb in liver, 150 ppb in kidney, and 200 ppb in fat. A tolerance refers to the concentration of marker residues in the target tissue used to monitor for total drug residues in the target animals. A safe concentration refers to the total residue concentration considered safe in edible tissues.

[52 FR 24995, July 2, 1987, as amended at 51 FR 12595, Mar. 28, 1989]

§ 556.740 Tylosin.

Tolerances are established for residues of tylosin in edible products of animals as follows:

- (a) In chickens and turkeys: 0.2 part per million (negligible residue) in uncooked fat, muscle, liver, and kidney.
- (b) In cattle: 0.2 part per million (negligible residue) in uncooked fat, muscle, liver, and kidney.
- (c) In swine: 0.2 part per million (negligible residue) in uncooked fat, muscle, liver, and kidney.
- (d) In milk: 0.05 part per million (negligible residue).
- (e) In eggs: 0.2 part per million (negligible residue).

§ 556.750 Virginiamycin.

Tolerances are established for negligible residues of virginiamycin in edible tissues of swine as follows:

- (a) Swine—
 - (1) 0.4 ppm in kidney, skin, and fat.
 - (2) 0.3 ppm in liver.
 - (3) 0.1 ppm in muscle.
- (b) Broiler chickens—
 - (1) 0.5 ppm in kidney.
 - (2) 0.3 ppm in liver.
 - (3) 0.2 ppm in skin and fat.
 - (4) 0.1 ppm in muscle.

(48 FR 18966, Mar. 27, 1981)

§ 556.760 Zeranol.

No residues of zeranol (6-(6,10-dihydroxyundecyl- β -resorcylic acid- μ -lactone) may be found in the uncooked edible tissues of cattle and sheep as determined by the following method of analysis:

I. METHOD OF ANALYSIS—ZERANOL

A gas chromatographic method for the determination of the drug in frozen beef tissue is described. Tissue is frozen and stored in a deep freezer until ready for examination. A weighed portion of wet tissue (with exception of fat) is homogenized and lyophilized to dry solid. The drug is recovered from dry tissue by an extraction with methanol in a Soxhlet extractor. The methanol extract is digested in the presence of hydrochloric acid to hydrolyze conjugates should any be present. Elimination of impurities is brought about by liquid partition transfer successively to chloroform to 1N sodium hydroxide, to carbon tetrachloride, to 1N sodium hydroxide, to ethyl ether, and, finally, to a dry residue. The residue is reacted with a silane mixture to create a volatile derivative which is quantitated by peak area measurements from a flame ionization detector. The drug can be detected at a level of 20 parts per billion with negligible interference from tissues or reagents.

II. REAGENTS

- A. Carbon tetrachloride, N.F., Fisher Scientific C-186, or equivalent.
- B. Chloroform, N.F., Fisher Scientific C-186, or equivalent.
- C. Chromatograph gases, flow rates adjusted to maximize sensitivity for specific chromatograph.
- D. Carrier gas, conventional tank helium.
- E. Flame makeup gas.
- F. Oxygen, conventional tank oxygen.
- G. Hydrogen, Linde high purity, or equivalent.
- H. Column packing, 3 percent GE SE-52 (Applied Science Laboratories) on P.E. Celite 60-80 mesh (Johns Manville Product No. 154-0048), or equivalent.
- I. Ether, anhydrous, Fisher Scientific E-10, or equivalent.
- J. Hexamethyldisilazane, Dow-Corning, Peninsular, or equivalent.
- K. Hydrochloric acid, analytical reagent grade.
- L. Methanol, certified A.C.S., spectranalyzed, Fisher Scientific A-408, or equivalent.
- M. Phosphoric acid, analytical reagent grade.
- N. Pyridine, anhydrous, A.C.S. reagent grade.

K. Silating reagent mixture: Pipet 8 milliliters each of pyridine and hexamethyldisilazane and 4 milliliters of trimethylchlorosilane into a clean glass vial with a polyethylene cap and mix thoroughly. Let stand overnight and decant supernatant liquid into a vial. Cap and store at room temperature for daily use. If kept dry, the reagent is stable for more than a month. Blanks are scanned by gas chromatography on each new bottle of J, F, and N material used in the silating reagent mixture for possible peak interference in the region of zeranol derivative.

L. Sodium chloride, analytical reagent grade.

M. Sodium hydroxide, analytical reagent grade.

N. Trimethylchlorosilane, Dow-Corning, Peninsular, or equivalent.

O. Water, distilled in glass.

P. Zeranol, primary standard.

Q. Solutions.

1. 2N Hydrochloric acid in water.
2. 3N Phosphoric acid in water.
3. 2 percent w/v sodium chloride in water.
4. 1N Sodium hydroxide in water.

III. APPARATUS

A. Extraction assemblies, Soxhlet, improved, standard taper grindings, Pyrex brand glass, 1,000 milliliters capacity, Sargent Catalog S-31265D, or equivalent.

B. Flasks, freeze drying, widemouth, 1,000 milliliters capacity, 24/40 standard taper grindings, Pyrex brand glass, Sargent Catalog S-28875-20-F, or equivalent.

C. Flasks, homogenizing, 250 milliliters, Sargent Catalog S-61716, or equivalent.

D. Funnels, separatory, Squibb stopper, with Teflon stopcock plug, Pyrex brand glass, 250- and 500-milliliter capacities, Sargent Catalog S-35815-20-F or G, or equivalent.

E. Gas chromatograph, P and M Model 5750 with flame ionization detector, or equivalent.

F. Gas chromatography column: Stainless steel tubing, 6 feet by $\frac{1}{8}$ inch packed with 3 percent by weight GE SE-52 (Applied Science Laboratories) deposited on P.E. Celite 60-80 mesh (product No. 154-0048), or equivalent. Condition the column by baking for 40-80 hours at 325° C. with a helium flow, but detached from the detector input. Injections of 1-2 microliters of a 50/50 mixture of hexamethyldisilazane and trimethylchlorosilane will help remove active sites in the column.

1. Prepare a TMS derivative of a 1,000-microgram zeranol standard as described in the procedure section. Inject 1-microliter quantities to determine whether the column is responding to the conditioning. After the column shows a response at the 1,000-microgram level, proceed to smaller quantities to optimize conditions.

2. The column and chromatograph must be conditioned to achieve a minimum sensitivity response so that a peak 5 millimeters in height results from an injection of 5 microliter of standard preparation containing 1 microgram of zeronol in the derivative preparation. This criterion must be met before tissue assay is attempted.

3. The column is brought to 250° C. after conditioning and held at that temperature for at least 12 hours before making a run.

G. Heating mantle, electric, Glas-Col, Sargent Catalog S-40866H, or equivalent.

H. Hot plate, with gradient rheostat heat control.

I. Meat grinder, manually operated or equivalent.

J. Steam bath.

K. Syringe, Hamilton Micro Syringe Model 701, 10-microliter capacity, or equivalent.

L. Torsion balance, 0.1 gram sensitivity, 500 grams capacity.

M. Vials, 1-dram glass with plastic tops, Owens-Illinois, Opticlear, or equivalent.

N. Virtis freeze drier, Sargent Catalog S-28881-80, or equivalent.

O. Virtis homogenizing mill, macro, Virtis No. 45, Sargent Catalog S-61700, or equivalent.

IV. STANDARD SOLUTIONS

A. Stock solution A: Accurately weigh 0.1000 gram of zeronol, primary standard, into a 250-milliliter beaker. Dissolve the standard in 80 milliliters of methanol and accurately dilute to 100 milliliters in a volumetric flask with methanol. By preparation, the solution contains 1,000 micrograms per milliliter.

B. Stock solution B: Dilute 10.0 milliliters of stock solution A to 100 milliliters with methanol to provide a standard containing 100 micrograms of the drug per milliliter.

C. Stock solution C: Dilute 5.0 milliliters of stock solution B to 100 milliliters with methanol to provide a standard of 5 micrograms per milliliter.

D. Stock solution D: Dilute 2.0 milliliters of stock solution B to 100 milliliters with methanol to provide a standard of 2 micrograms per milliliter. Transfer 1.0 milliliter of stock solution D to a 1-dram glass vial, evaporate to a dry residue in a vacuum desiccator at reduced pressure. The residue contains 2 micrograms of zeronol to be used as a calibration standard in operation of the gas chromatograph.

V. PROCEDURE

A. Preparation of glassware: Glassware should be washed in detergent or chromic acid solution to remove contaminants and rinsed in water to remove traces of cleaning agent. Rinse with methanol before using.

B. Preparation of sample.

1. Collect muscle, liver, kidney, and testis from a freshly sacrificed animal under the cleanest conditions possible.

2. Grind the fresh tissue in a meat grinder, divide into 100-gram portions, and wrap in aluminum foil. Store wrapped tissue in deep freeze. Fat should be wrapped in foil and stored in deep freeze.

C. Extraction procedure for muscle, kidney, and tripe.

1. Weight 100 grams of partially thawed tissue into a 250-milliliter homogenization flask, add 60 milliliters of water, and attach to a Virtis "45" Tissue Mill, or equivalent.

2. Mix the materials at 45,000 r.p.m. for 10 minutes to obtain a thin homogenate.

3. Transfer the homogenate to a 1-liter wide-mouth, freeze drying flask using 10 milliliters of water for a rinse.

4. Place the flask on its side in a new horizontal position in a slurry of dry ice and acetone. Rotate the flask on its side as the homogenate cools to set down a uniform frozen solid layer on the wall of the flask.

5. Mount the flask on a Virtis freeze drier, or equivalent, and lyophilize to dry solid. This operation usually requires 20-24 hours.

Stopping place.

6. Transfer the solid cake to a clean sheet of paper and crumble by hand to a size convenient for transfer to an extraction thimble.

7. Transfer the solids to a single thick-walled 60 x 180 milliliter Soxhlet extraction thimble and compact the solids sufficiently to guarantee complete immersion during extraction.

8. Transfer 600 milliliters of methanol to a 1-liter pot of a Soxhlet extraction assembly and place the thimble in the extractor. Mount a large glass funnel in the neck of the extractor with the stem extending into the thimble. Rinse the 1-liter freeze drying flask with three 50-milliliter portions of fresh methanol and transfer the rinse through the funnel into the thimble. Mount the condenser in the extractor and extract the solids for 15 hours. The extractor should be heated with the electric heating mantle so that a fill-empty cycle requires 18-24 minutes.

9. Drain the methanol from the thimble. Composite the methanol from the extractor and pot in an 800-milliliter beaker.

10. Rinse the pot with 10 milliliters of methanol and add to the methanol composite. Transfer 50 milliliters of 2N HCl down the pot side wall, and add to methanol composite. Concentrate to 125 milliliters by boiling on a hot plate.

D. Extraction procedure for fat.

1. Cut fat into ¼-inch cubes. The lyophilization of fat is unnecessary since it is essentially water free.

2. Transfer 100 grams of the prepared fat to a 60- x 180-millimeter extraction thimble.

and extract with 750 milliliters of methanol for 15 hours in the Soxhlet extractor. The extractor should be heated with the electric heating mantle so that a fill-empty cycle requires 18-24 minutes.

3. Drain the methanol from the thimble. Composite the methanol from the extractor and pot into an 800-milliliter beaker.

4. Rinse the pot with 10 milliliters of methanol and add to the methanol composite. Transfer 50 milliliters of 2N HCl down the pot side wall, and add to methanol composite. Concentrate to 125 milliliters by boiling on a hot plate.

E. Solvent partition.

1. Transfer the methanol concentrate to a 500-milliliter separatory funnel, identified by number as 1, with 70 milliliters of chloroform rinse and mix.

2. Add 300 milliliters of water and without shaking allow liquid phases to separate.

3. Withdraw the chloroform layer into a separatory funnel, identified by number as 2, containing 100 milliliters of 2 percent aqueous sodium chloride.

4. Gently mix the contents of funnel 2 horizontally end to end 30 times and allow phases to separate. Usually about 20 minutes are required to obtain maximum chloroform separation.

5. Withdraw the chloroform layer into a beaker.

6. Extract with shaking the contents of funnels 1 and 2 successively with three more 50-milliliter portions of chloroform.

7. Composite the chloroform extracts and concentrate to 125 milliliters by evaporation on a steam bath and cool to room temperature.

8. Transfer the chloroform composite to a 250-milliliter separatory funnel, fitted with a Teflon stopcock, using 10 milliliters of chloroform as a rinse.

9. Extract the chloroform with three separate 20-milliliter portions of 1N sodium hydroxide solution retaining the emulsion in the sodium hydroxide phase. Agitation of sodium hydroxide with the chloroform extract for the first time is accompanied by the appearance of emulsion.

10. Perform an extraction by gently inverting the closed funnel and returning the funnel to an upright position.

11. Repeat phase mixing 30 times per extraction.

12. Allow phases to separate for 10 minutes. The time delay allows for gradual dissipation of the emulsion to improve phase separation. The zanol transfers from the chloroform to the upper sodium hydroxide phase in this operation.

13. Composite the sodium hydroxide extracts.

14. Wash the sodium hydroxide extract with three 50-milliliter portions of chloroform using the technique as in step 9 and the same 10-minute interval for phase separation.

Washing the chloroform removes the emulsion and unwanted impurities from the sodium hydroxide phase.

15. Discard the chloroform washes. Transfer the sodium hydroxide extracts to a 250-milliliter beaker. Rinse each separatory funnel with two 5-milliliter portions of water and add to the sodium hydroxide extract. Wash each funnel twice with tap water and twice with distilled water before next use.

16. Neutralize the washed sodium hydroxide extract to pH 8.0 by dropwise addition of 3N phosphoric acid using a pH meter for pH detection.

17. Transfer the pH 8.0 water extract to a 250-milliliter separatory funnel using 10 to 20 milliliters of water for a rinse.

18. Extract the solution with three separate 50-milliliter portions of carbon tetrachloride. The zanol transfers to the lower carbon tetrachloride phase. Use the same 30-count phase-mixing technique as in step 9 and allow the mixture to stand 5 minutes for phase separation.

19. Composite the carbon tetrachloride extracts.

20. Extract the carbon tetrachloride composite with two 20-milliliter portions of 1N sodium hydroxide. Zanol transfers from carbon tetrachloride to the upper sodium hydroxide phase. After phase mixing, allow the mixture to stand 5 minutes for phase separation.

21. Composite the sodium hydroxide extracts.

22. Wash the extract with two 50-milliliter portions of carbon tetrachloride. Allow the mixture to stand 5 minutes for phase separation. Discard the carbon tetrachloride washes.

23. Transfer the sodium hydroxide extract into a 250-milliliter beaker. Rinse the separatory funnel with two 5-milliliter portions of water and add to the sodium hydroxide extract. Wash each funnel twice with tap water and twice with distilled water before next use. Adjust the sodium hydroxide extract to a pH of 9.5 by dropwise addition of 3N phosphoric acid and transfer to a 250-milliliter separatory funnel using 10-20 milliliters of water for a rinse.

24. Extract the pH 9.5 water solution with three separate 30-milliliter portions of anhydrous ethyl ether. Allow the mixture to stand 5 minutes for phase separation. The zanol transfers to the upper ether phase.

25. Composite the ether extracts in a 125-milliliter Erlenmeyer flask.

26. Reduce the volume of ether to about 1-2 milliliters by evaporation on a hot plate with low heat while removing vapor from top of flask by vacuum aspiration.

27. Transfer ether residue to a 1-dram glass vial. Rinse down flask side wall with 1-

2 milliliters of fresh ether and transfer to the glass vial.

28. Continue evaporation of ether to 0.1 milliliter.

29. Place vial in a vacuum desiccator and evaporate residue at line vacuum and room temperature overnight to dryness.

30. Close vial with a plastic cap and submit ether residue for preparation of TMS derivative and gas chromatographic assay. *Stopping place.*

F. Gas liquid chromatography.

1. Start the gas chromatography and maintain the following operational conditions:

Carrier gas pressure: 50 p.s.i. at tank.

Carrier gas flow rate: Sufficient to give zeranol derivative peak a retention time of 4-8 minutes.

Electrometer range: 10^2 or 10^1 .

Detector temperature: 325° C.

Injection port temperature: 325° C.

Column temperature: 250°-280° C., operate isothermally.

Recorder sensitivity: 1 millivolt.

Recorder chart speed: 1 inch per minute.

Sample size: 1 microliter to 5 microliters as necessary to give desired peak area for quantitative measurement.

Septums: Replace each evening and allow to condition overnight at operational temperature.

Flame assembly: Remove silica ash from the flame assembly each week. The flame assembly is removed; the anode, flame jet, and chimney are cleaned with a nylon bristle brush. Water and acetone are drawn through the jet capillary to remove any foreign material.

2. Add 0.2 milliliter of silylating reagent to the sample or to the zeranol standard.

3. Stopper the vial and shake vigorously.

4. Warm the vial at 40°-50° C. for a few minutes, then roll the vial on a horizontal plane to insure that all of the interior surfaces of the vial have been in contact with the reagent.

5. Let vial stand for 4 hours or overnight in a warm area (40° C.) to allow reaction to reach completion.

6. Place vial in a small padded centrifuge tube and centrifuge to settle the precipitate and insure that all the liquid is at the bottom of the vial.

7. Inject 1.0-5.0 microliters of clear solution into the chromatograph. At the beginning of the day's run, make 3-5 injections of a standard to condition the column for that day before taking quantitative data.

8. Run known mixtures at the beginning, middle, and end of the day's run over the concentration range of samples to be analyzed to compensate for day-to-day sensitivity fluctuations and drift. If four or less samples are to be run, calibrating at the beginning and end of the run is sufficient.

VI. CALCULATIONS

Area values are obtained on known mixtures and samples by multiplying the net peak height by the peak width at half height or by counting squares. Area values obtained on knowns are plotted versus zeranol concentration. Calibration plots indicate a near linear function in the 0-10 microgram range. Area values obtained on samples are converted directly to microgram quantities using the curve. Control tests demonstrated a 70 percent recovery of zeranol from spiked wet beef liver and muscle necessitating a correction factor.

Zeranol, parts per billion =

Micrograms of zeranol found $\times 1,000$

$W \times 0.7$

Where:

0.7 = Correction factor for 70 percent recovery.

W = Grams of tissue examined.

VII. RECOVERY STUDY

A. Fortification of reagent blank.

1. For those using this method for the first time either for recovery study or tissue assay, a solvent blank and solvent fortified with zeranol should be processed through the entire procedure. This preliminary operation will establish whether or not the procedure is free from contamination arising from solvents and glassware and demonstrate the level of recovery of the standard zeranol. Level of recovery should be in the same range as the samples.

2. Transfer 600 milliliters of methanol to a 1-liter beaker. Add 50 milliliters of 2N HCl to the methanol and concentrate to 125 milliliters by boiling on a hot plate.

3. Transfer 600 milliliters of methanol to a 1-liter beaker. Add 50 milliliters of 2N HCl to the methanol and concentrate to 125 milliliters by boiling on a hot plate. Spike the concentrate with 1.0 milliliter of stock solution D.

4. Assay both samples as described in the procedure beginning extraction step V-E1.

B. Fortification of samples.

1. Transfer 100-gram portions of partially thawed tissues into 250-milliliter homogenizing flasks and set half of them aside to serve as tissue blanks.

2. Add to the remaining samples 1 milliliter of stock solution D to serve as fortified samples to which 20 parts per billion zeranol have been added.

3. Assay both fortified and unfortified tissue as described in the procedure section beginning with V-C1.

§ 558.770 Zoalene.

Tolerances are established for residues of zoalene (3,5-dinitro-o-toluidide) and its metabolite 3-amino-5-nitro-o-toluidide in food as follows:

(a) In edible tissues of chickens:

(1) 6 parts per million in uncooked liver and kidney.

(2) 3 parts per million in uncooked muscle tissue.

(3) 2 parts per million in uncooked fat.

(b) In edible tissues of turkeys: 3 parts per million in uncooked muscle tissue and liver.

PART 558—NEW ANIMAL DRUGS FOR USE IN ANIMAL FEEDS

Subpart A—General Provisions

Sec.

558.3 Definitions and general considerations applicable to this part.

558.4 Medicated feed applications.

558.5 New animal drug requirements for liquid Type B feeds.

558.15 Antibiotic, nitrofurans, and sulfonamide drugs in the feed of animals.

558.20 Drugs used in medicated feeds in use before January 1, 1958, which are not otherwise listed; Interim listing.

Subpart B—Specific New Animal Drugs For Use in Animal Feeds

- 558.35 Aklomide.
- 558.52 Amprolium.
- 558.58 Amprolium and ethopabate.
- 558.59 Apramycin.
- 558.60 Arsanilate sodium.
- 558.62 Arsanilate acid.
- 558.76 Bacitracin methylene disalicylate.
- 558.78 Bacitracin, zinc.
- 558.95 Bambermycins.
- 558.105 Buquinolate.
- 558.115 Carbadox.
- 558.120 Carbarsone (not U.S.P.).
- 558.126 Chlortetracycline.
- 558.145 Chlortetracycline, procaine penicillin, and sulfamethazine.
- 558.155 Chlortetracycline, procaine penicillin, and sulfathiazole.
- 558.175 Clopidol.
- 558.185 Coumaphos.
- 558.195 Decoquinolate.
- 558.205 Dichlorvos.
- 558.248 Erythromycin thiocyanate.
- 558.254 Famphur.
- 558.258 Fenbendazole.
- 558.262 Furazolidone.
- 558.265 Halofuginone hydrobromide.

Sec.

- 558.274 Hygromycin B.
- 558.295 Iodinated casein.
- 558.311 Lasalocid.
- 558.315 Levamisole hydrochloride (equivalent).
- 558.325 Lincomycin.
- 558.340 Maduramicin ammonium.
- 558.342 Melengestrol acetate.
- 558.348 Mibolerone.
- 558.355 Monensin.
- 558.360 Morantel tartrate.
- 558.363 Narasin.
- 558.365 Nequinat.
- 558.366 Nicarbazine.
- 558.367 Niclosamide.
- 558.369 Nitarsone.
- 558.370 Nitrofurazone.
- 558.376 Nitromide and sulfantran.
- 558.415 Novobiocin.
- 558.430 Nystatin.
- 558.435 Oleandomycin.
- 558.450 Oxytetracycline.
- 558.460 Penicillin.
- 558.464 Poloxalene.
- 558.465 Poloxalene free-choice liquid Type C feed.
- 558.485 Pyrantel tartrate.
- 558.515 Robenidine hydrochloride.
- 558.525 Ronnel.
- 558.530 Roxarsone.
- 558.550 Salinomycin.
- 558.565 Styrylpyridinium chloride, diethyl-carbamazine.
- 558.575 Sulfadimethoxine, ormetoprim.
- 558.579 Sulfathoxypyridazine.
- 558.582 Sulfamerazine.
- 558.586 Sulfaminoxoline.
- 558.600 Tiamulin.
- 558.615 Thiabendazole.
- 558.625 Tylosin.
- 558.630 Tylosin and sulfamethazine.
- 558.635 Virginiamycin.
- 558.680 Zoalene.

AUTHORITY: Sec. 512, 82 Stat. 343-351 (21 U.S.C. 360b); 21 CFR 5.10 and 5.83.

SOURCE: 40 FR 13959, Mar. 27, 1975, unless otherwise noted.

Subpart A—General Provisions

§ 558.3 Definitions and general considerations applicable to this part.

(a) Regulations in this part provide for approved uses of drugs and combinations of drugs in animal feeds. Approved combinations of such drugs are specifically identified or incorporated by cross-reference. Unless specifically provided for by the regulations, a combination of two or more drugs is not approved.

(b) The following definitions apply to terms used in this part:

(1) New animal drugs for use in animal feed are placed in two categories as follows:

(i) Category I—These drugs require no withdrawal period at the lowest use level in each species for which they are approved.

(ii) Category II—These drugs require a withdrawal period at the lowest use level for at least one species for which they are approved or are regulated on a "no-residue" basis or with a "zero" tolerance because of a carcinogenic concern regardless whether a withdrawal period is required.

(2) A "Type A medicated article" is intended solely for use in the manufacture of another Type A medicated article or a Type B or Type C medicated feed. It consists of a new animal drug(s), with or without carrier (e.g., calcium carbonate, rice hull, corn, gluten) with or without inactive ingredients. The manufacture of a Type A medicated article requires an application approved under § 514.105(a) of this chapter.

(3) A "Type B medicated feed" is intended solely for the manufacture of other medicated feeds (Type B or Type C). It contains a substantial quantity of nutrients including vitamins and/or minerals and/or other nutritional ingredients in an amount not less than 25 percent of the weight. It is manufactured by diluting a Type A medicated article or another Type B medicated feed. The maximum concentration of animal drug(s) in a Type B medicated feed is 200 times the highest continuous use level for Category I drugs and 100 times the highest continuous use level for Category II drugs. The term "highest continuous use level" means the highest dosage at which the drug is approved for continuous use (14 days or more), or, if the drug is not approved for continuous use, it means the highest level used for disease prevention or control. If the drug is approved for multiple species at different use levels, the highest approved level of use would govern

under this definition. The manufacture of a Type B medicated feed from a Category II, Type A medicated article requires an application approved under § 514.105(b) of this chapter.

(4) A "Type C medicated feed" is intended as the complete feed for the animal or may be fed "top dressed" (added on top of usual ration) or offered "free-choice" (e.g., supplement) in conjunction with other animal feed. It contains a substantial quantity of nutrients including vitamins, minerals, and/or other nutritional ingredients. It is manufactured by diluting a Type A medicated article or a Type B medicated feed may be further diluted to produce another type C medicated feed. The manufacture of a Type C medicated feed from a Category II, Type A medicated article requires an application approved under § 514.105(b) of this chapter.

(5) A Type B or Type C medicated feed manufactured from a drug component (bulk or "drum-run" (dried crude fermentation product)) requires an application approved under § 514.105(a) of this chapter.

(51 FR 7392, Mar. 3, 1986, as amended at 51 FR 2682, Jan. 26, 1987)

§ 558.4 Medicated feed applications.

(a) The manufacture of a Type B or Type C medicated feed from a Category I, Type A medicated article is exempt from the requirement of an approved medicated feed application.

(b) The manufacture of a Type B or Type C medicated feed from a Category II, Type A medicated article requires an approved medicated feed application.

(c) The use of Type B and Type C medicated feeds shall conform to the conditions of use provided for in Subpart B of this part and in §§ 510.513, 558.15, and 558.20.

(d) This paragraph identifies each drug by category, the maximum level of drug in Type B medicated feeds, and the assay limits for the drug in Type A medicated articles and Type B and Type C medicated feeds, as follows:

CATEGORY I

Drug	Assay limits percent ¹ type A	Type B maximum (200x)	Assay limits percent ¹ type B/C ²
Alkamide	90-110	22.75 g/lb (5.0%)	85-120.
Amprolium with Ethopabate	94-114	22.75 g/lb (5.0%)	80-120.
Bacitracin methylene disalicylate	85-115	25.0 g/lb (5.5%)	70-130.
Bacitracin zinc	84-115	5.0 g/lb (1.1%)	70-130.
Bambermycin	90-110	800 g/ton (0.09%)	80-120/70-130.
Buquinolate	90-110	9.8 g/lb (2.2%)	80-120.
Chlortetracycline	85-115	40.0 g/lb (8.8%)	80-115/70-130.
Coumaphos	95-115	8.0 g/lb (1.3%)	80-120.
Decoquinolate	90-105	2.72 g/lb (0.6%)	80-120.
Dichlorol	100-115	33.0 g/lb (7.3%)	90-120/80-130.
Erythromycin (thiocyanate salt)	85-115	9.25 g/lb (2.04%)	<20g/ton 70-115/150-50; >20g/ton 75-125.
Iodinated casein	85-115	20.0 g/lb (4.4%)	75-125.
Lasaloid	100-120	40.0 g/lb (8.8%)	Type B (cattle and sheep): 80-120; Type C (all): 75-125.
Monensin	90-110	40.0 g/lb (8.8%)	Chickens, turkeys, and quail: 75-125; Cattle: 5-10 g/ton 80-120; Cattle: 10-30 g/ton 85-115; Lq. feed: 80-120.
Narsin	90-110	7.2 g/lb (1.6%)	85-115/75-125.
Nequinolate	95-112	1.83 g/lb (0.4%)	80-120.
Nicosamide	85-120	225g/lb (49.5%)	80-120.
Nystatin	85-125	5.0 g/lb (1.1%)	75-125.
Oleandomycin	85-120	1.125 g/lb (0.25%)	<11.25 g/ton 70-130; >11.25 g/ton 75-125.
Oxytetracycline	90-120	20.0 g/lb (4.4%)	75-125/65-135.
Penicillin	80-120	10.0 g/lb (2.2%)	65-135.
Penicillin	80-120	1.5 g/lb (0.33%)	65-135.
Streptomycin	85-115	7.5 g/lb (1.65%)	70-130.
Poloxalene	90-110	54.48 g/lb (12.0%)	Liq. feed: 85-115.
Saltomycin	100-120	6.0 g/lb (1.3%)	80-120.
Tiamulin	113.4 g/lb, 100-108 5 and 10 g/lb, 90-115	3.5 g/lb (0.8%)	80-115.
Tylosin	90-120	10.0 g/lb (2.2%)	75-125.
Virginiamycin	85-115	10.0 g/lb (2.2%)	70-130.
Zonalene	98-104	11.35 g/lb (2.5%)	85-115.

¹ Percent of labeled amount.² Values given represent ranges for either Type B or Type C medicated feeds. For those drugs that have two range limits, the first set is for a Type B medicated feed and the second set is for a Type C medicated feed. These values (ranges) have been assigned in order to provide for the possibility of dilution of a Type B medicated feed with lower assay limits to make Type C medicated feed.

CATEGORY II

Drug	Assay limits percent ¹ Type A	Type B maximum (100x)	Assay limits percent ¹ Type B/C ²
Amprolium	94-114	11.35 g/lb (2.5%)	80-120.
Apramycin	88-112	7.5 g/lb (1.65%)	80-120.
Asanilate sodium	90-110	4.5 g/lb (1.0%)	85-115/75-125.
Asanilate acid	90-110	4.5 g/lb (1.0%)	85-115/75-125.
Butylurate	90-110	17.0 g/lb (3.74%)	85-115.
Butylurate	90-110	63.45 g/lb (14.0%)	85-115.
Piperazine	90-110	49.85 g/lb (11.0%)	85-115.
Phenothiazine	90-110	263.32 g/lb (58.0%)	85-115.
Carbadox	90-110	2.5 g/lb (0.55%)	75-125.
Carbadox	93-102	17.0 g/lb (3.74%)	85-115.
Clopidol	94-106	11.4 g/lb (2.5%)	90-115/80-120.
Emphur	100-110	5.5 g/lb (1.21%)	90-115/80-120.
Fenbendazole	93-113	8.87 g/lb (1.96%)	75-125.
Furazolidone	95-105	10.0 g/lb (2.2%)	85-115.

CATEGORY II—Continued

Drug	Assay limits percent ¹ Type A	Type B maximum (100x)	Assay limits percent Type B/C ²
Halofuginone hydrobromide	80-120	272.0 g/ton (0.03%)	70-125
Hygromycin B	90-110	1,200 g/ton (0.13%)	75-125
Levamisole	85-120	113.5 g/lb (25%)	85-125
Lincomycin	90-115	10.0 g/lb (2.2%)	80-130
Maduramicin ammonium	90-110	54.5 g/ton (0.006%)	80-120
Melengestrol acetate	90-110	2.0 g/ton (0.00022%)	70-120
Morantel tartrate	90-110	66.0 g/lb (14.52%)	85-115
Neomycin	80-120	7.0 g/lb (1.54%)	70-125
Neomycin	85-120	7.0 g/lb (1.54%)	70-125
Oxytetracycline	80-120	10.0 g/lb (2.2%)	65-135
Nicarbazin (granular)	90-110	5.675 g/lb (1.25%)	85-115/75-125
Nerazin	90-110	5.675 g/lb (1.25%)	85-115/75-125
Nicarbazin (powder)	98-106	5.675 g/lb (1.25%)	85-115/80-120
Nitarsone	90-110	8.5 g/lb (1.87%)	85-120
Nitrofurazone	90-110	10.0 g/lb (2.2%)	80-125
Nitrofurantoin	90-110	11.35 g/lb (2.5%)	80-120
Sulfanilic acid	85-115	13.6 g/lb (3.0%)	75-125
Nitrofurantoin	90-110	11.35 g/lb (2.5%)	85-115
Sulfanilic acid	85-115	5.65 g/lb (1.24%)	75-125
Roxarsone	95-103	2.275 g/lb (0.5%)	85-120
Novobiocin	85-115	17.5 g/lb (3.85%)	80-120
Phenothiazine	90-110	66.5 g/lb (14.6%)	85-115
Piperazine	90-110	165 g/lb (40.25%)	85-115
Pyrantel tartrate	90-110	4.6 g/lb (1.1%)	75-125
Robenidine	95-115	1.5 g/lb (0.33%)	80-120
Ronnel	85-115	27.2 g/lb (6.0%)	80-120
Roxarsone	95-103	2.275 g/lb (0.5%)	85-120
Roxarsone	95-103	2.275 g/lb (0.5%)	85-120
Aklomide	90-110	11.35 g/lb (2.5%)	85-120
Roxarsone	95-103	2.275 g/lb (0.5%)	85-120
Clopidol	84-106	11.35 g/lb (2.5%)	80-120
Bacitracin methylene disalicylate	85-115	5.0 g/lb (1.1%)	70-130
Roxarsone	95-103	2.275 g/lb (0.5%)	85-120
Monensin	90-110	5.5 g/lb (1.2%)	75-125
Sulfadimethoxine	95-115	5.675 g/lb (1.25%) 0.01% (combined)	85-115/75-125
Ormetoprim (5/3)	95-115	3.405 g/lb (0.75%) 0.02% (combined)	85-115
Sulfadimethoxine	95-115	85.1 g/lb (18.75%)	85-115/75-125
Ormetoprim (5/1)	95-115	17.0 g/lb (3.75%)	85-115
Sulfathiazole	95-105	50.0 g/lb (11.0%)	85-115
Sulfamerazine	85-115	18.6 g/lb (4.0%)	85-115
Sulfamethazine	95-115	10.0 g/lb (2.2%)	80-120
Chlortetracycline	85-115	10.0 g/lb (2.2%)	85-125/70-130
Penicillin	85-115	5.0 g/lb (1.1%)	85-125/70-130
Sulfamethazine	85-115	10.0 g/lb (2.2%)	80-120
Chlortetracycline	85-115	10.0 g/lb (2.2%)	85-125/75-130
Sulfamethazine	85-115	10.0 g/lb (2.2%)	80-120
Tylosin	80-120	10.0 g/lb (2.2%)	75-125
Sulfanilic acid	85-115	13.6 g/lb (3.0%)	75-125
Aklomide	90-110	11.2 g/lb (2.5%)	85-120
Sulfanilic acid	85-115	13.6 g/lb (3.0%)	75-125
Aklomide	90-110	11.2 g/lb (2.5%)	85-120
Roxarsone	95-103	2.715 g/lb (0.60%)	85-120
Sulfanilic acid	85-115	13.6 g/lb (3.0%)	75-125
Aklomide	90-110	11.2 g/lb (2.5%)	85-120
Roxarsone	95-103	2.27 g/lb (0.5%)	85-120
Sulfathiazole	98-106	11.2 g/lb (2.5%)	85-115
Sulfathiazole	85-115	10.0 g/lb (2.2%)	80-120
Chlortetracycline	85-125	10.0 g/lb (2.2%)	70-130
Penicillin	80-120	5.0 g/lb (1.1%)	70-130
Thiabendazole	94-106	45.4 g/lb (10.0%)	<7% 85-115; >7% 110

¹ Percent of labeled amount.² Values given represent ranges for either Type B or Type C medicated feeds. For those drugs that have two range lists the first set is for a Type B medicated feed and the second set is for a Type C medicated feed. These values (ranges) have been assigned in order to provide for the possibility of dilution of a Type B medicated feed with lower assay limits to make a Type C medicated feed.

(e) When drugs from both categories are in combination, the Category II requirements will apply to the combination drug product.

[51 FR 7392, Mar. 3, 1986, as amended at 52 FR 2862, Jan. 26, 1987; 52 FR 7834, Mar. 13, 1987; 52 FR 25213, July 6, 1987; 52 FR 26954, July 17, 1987; 52 FR 39912, Oct. 26, 1987; 53 FR 14788, Apr. 26, 1988; 53 FR 25182, July 5, 1988; 53 FR 40060, Oct. 13, 1988; 54 FR 1686, Jan. 17, 1989; 54 FR 1928, Jan. 18, 1989; 54 FR 5229, Feb. 2, 1989; 54 FR 9430, Mar. 7, 1989]

§ 558.5 New animal drug requirements for liquid Type B feeds.

(a) Information available to the Commissioner of Food and Drugs shows that certain drugs are unstable when added to some liquid Type B medicated feeds. The demonstrated instability of these drugs gives rise to the question of the stability of other drugs when added to liquid Type B medicated feeds, except where specific approval has been granted for such use. Therefore, the labeling of a drug to provide for its use in a liquid Type B medicated feed causes the drug to be a new animal drug for such use for which an approved new animal drug application is required pursuant to section 512(b) of the Federal Food, Drug, and Cosmetic Act.

(b) The addition of a drug to a liquid Type B medicated feed causes such Type B feed to become an animal feed bearing or containing a new animal drug for which an approved application is required pursuant to section 512(m) of the act.

(c) Each drug product, intended for oral administration to animals, which contains any of the drugs listed in paragraph (d) of this section and which bears labeling for its use in animal feed and/or drinking water shall also include in such labeling the following statement: "FOR USE IN ONLY. NOT FOR USE IN LIQUID TYPE B MEDICATED FEEDS," the blank being filled in with the words "DRY FEEDS," "DRINKING WATER," "DRY FEEDS AND DRINKING WATER" applicable, unless:

(1) Such drug product is the subject of an approved new animal drug application providing for its use in liquid Type B medicated feeds, or;

(2) The labeling provisions of this paragraph have been waived on the basis of approval of a petition which includes a copy of the product label; a description of the formulation; and information which establishes that the physical, chemical, or other properties of the particular drug product are such that it cannot reasonably be expected to be diverted for use in liquid Type B medicated feeds. Such petitions shall be submitted to the Food and Drug Administration, Center for Veterinary Medicine, 5600 Fishers Lane, Rockville, Md. 20857.

(d) The labeling provisions of paragraph (c) of this section apply to all forms of bacitracin, oxytetracycline, and chlortetracycline.

(e) For any drug which is the subject of an approved new animal drug application, the labeling provisions of paragraph (c) of this section may be implemented without prior approval as provided for in § 514.8(d) and (e) of this chapter.

[40 FR 13959, Mar. 27, 1975, as amended at 52 FR 2684, Jan. 26, 1987]

§ 558.15 Antibiotic, nitrofurans, and sulfonamide drugs in the feed of animals.

(a) The Commissioner of Food and Drugs will propose to revoke currently approved subtherapeutic (increased rate of gain, disease prevention, etc.) uses in animal feed of antibiotic and sulfonamide drugs whether granted by approval of new animal drug applications, master files and/or antibiotic or food additive regulations, by no later than April 20, 1975, or the nitrofurans drugs by no later than September 5, 1975, unless data are submitted which resolve conclusively the issues concerning their safety to man and animals and their effectiveness under specific criteria established by the Food and Drug Administration based on the guidelines included in the report of the FDA task force on the use of antibiotics in animal feeds. All persons or firms previously marketing identical, related, or similar products except the nitrofurans drugs not the subject of an approved new animal drug application must submit a new animal drug application by July 19, 1973, or by December 4, 1973, in the case of nitrofurans

drugs, if marketing is to continue during the interim. New animal drug entities with antibacterial activity not previously marketed, now pending approval or submitted for approval prior to, on, or following the effective date of this publication, shall satisfy such criteria prior to approval.

(b) Any person interested in developing data which will support retaining approval for such uses of such antibiotic, nitrofurantoin, and sulfonamide drugs pursuant to section 512(l) of the Federal Food, Drug, and Cosmetic Act shall submit to the Commissioner the following:

(1) By July 19, 1973, records and reports of completed, ongoing, or planned studies, including protocols, on the tetracyclines, streptomycin, dihydrostreptomycin, penicillin, and the sulfonamides; for all other antibiotics by October 17, 1973; and for the nitrofurantoin drugs by March 4, 1974. The Food and Drug Administration encourages sponsors to consult with the Center for Veterinary Medicine on protocol design and plans for future studies.

(2) By April 20, 1974, data from completed studies on the tetracyclines, streptomycin, dihydrostreptomycin, the sulfonamides, and penicillin assessing the effect of the subtherapeutic use of the drug in feed on the salmonella reservoir in the target animal as compared to that in nonmedicated controls. Failure to complete the salmonella studies for any of these drugs by that time will be grounds for proceeding to immediately withdraw approval.

(3) By April 20, 1975, data satisfying all other specified criteria for safety and effectiveness, including the effect on the salmonella reservoir for any antibiotic or sulfonamide drugs and by September 5, 1975, for the nitrofurantoin drugs, approved for subtherapeutic use in animal feeds. Drug efficacy data shall be submitted for any feed-use combination product containing such drug and any feed-use single ingredient antibiotic, nitrofurantoin, or sulfonamide not reviewed by the National Academy of Sciences—National Research Council, Drug Efficacy Study covering drugs marketed between 1938 and 1962.

(4) Progress reports on studies underway every January 1 and July 1 until completion.

(c) Failure on the part of any sponsor to comply with any of the provisions of paragraph (b) of this section for any of the antibacterial drugs included in paragraph (b)(1) of this section, or interim results indicating a health hazard, will be considered as grounds for immediately proceeding to withdraw approval of that drug for use in animal feeds under section 512(l) of the act in the case of failure to submit required records and reports and under section 512(e) where new information shows that such drug is not shown to be safe.

(d) Criteria based upon the guidelines laid down by the task force may be obtained from the Food and Drug Administration, Center for Veterinary Medicine, 5600 Fishers Lane, Rockville, MD 20857.

(e) Reports as specified in this section shall be submitted to: Food and Drug Administration, Center for Veterinary Medicine, Office of New Animal Drug Evaluation (HPV-100) 5600 Fishers Lane, Rockville, MD 20857.

(f) Following the completion of the requirements of paragraphs (a) and (b) of this section and the studies provided for therein:

(1) Those antibiotic, nitrofurantoin, and sulfonamide drugs which fail to meet the prescribed criteria for subtherapeutic uses but which are found to be effective for the therapeutic purposes will be permitted in feed only for high-level, short-term therapeutic use and only by or on the order of a licensed veterinarian.

(2) Animal feeds containing antibacterial drugs permitted to remain in use for subtherapeutic purposes shall be labeled to include a statement of the quantity of such drugs.

(g) The submission of applications and data required by paragraphs (a) and (b) of this section is not required for the continued manufacture of any Type B feed which is produced solely from a Type A article that is in compliance with the requirements of this section: *Provided*, That the Type B feed contains no drug ingredients whose use in or on animal feed is

quires an approved application pursuant to section 512(m) of the act and/or where the Type A article is approved by regulation in this part.

(1) The following antibacterial Type A articles manufactured by the design-

nated sponsors are eligible for interim marketing based on their compliance with the requirements of this section:

Drug sponsor	Type A article	Species	Use levels	Indications for use
Pfizer-Moore, Inc.	Bacitracin zinc	Chickens, turkeys, swine, pheasants, quail, and cattle.	Sec. 558.78.	Sec. 558.78.
A. L. Laboratories, Inc.	do	Chickens, turkeys, pheasants, and quail.	do	Do.
A. L. Laboratories, Inc., SDS Batch Corp.	Bacitracin methylene disalicylate.	Chicken turkeys, swine, and cattle.	Sec. 558.78.	Sec. 558.78.
Esco Products Co.	Hygromycin B	Chickens and swine.	Sec. 558.274.	Sec. 558.274.
Do	Tylosin	Chickens, swine, and beef cattle.	Sec. 558.625.	Sec. 558.625.
W. Laboratories, Inc.	Erythromycin	Chickens, turkeys, and swine.	Sec. 558.248.	Sec. 558.248.
He Upjohn Co.	Lincomycin	Chickens.	Sec. 558.325.	Sec. 558.325.
Bas, Inc.	Oleandomycin	Chickens, turkeys, and swine.	Sec. 558.435.	Sec. 558.435.
Sechel-Roussel Agri-Vet, Inc.	Bambermycine.	Chickens.	Sec. 558.95.	Sec. 558.95.
Esco Products Co.	Tylosin and sulfamethazine.	Swine.	Sec. 558.630.	Sec. 558.630.
Merck & Co., Inc., SDS Batch Corp., Hess & Clark, Pfizer, Inc., and VPO, Inc.	Chlortetracycline.	Chickens, turkeys, swine, and cattle.	Sec. 558.128.	Sec. 558.128.
Reed Sharp & Dohme Research Labs., and Solvay Veterinary, Inc.	Procaine Penicillin.	Chickens, turkeys, swine, pheasants, and quail.	Sec. 558.480.	Sec. 558.480.
Do, Inc., VPO, Inc., and Farnam Mills, Inc.	Oxytetracycline.	Chickens and turkeys.	Sec. 558.450.	Sec. 558.450.
Do	do	Swine (10 to 30 lb).	25 to 50 g/ton.	To increase rate of gain and improve feed efficiency.
Do	do	Swine (30 to 200 lb).	7½ to 10 g/ton.	Do.
Do	do	Swine	50 g/ton.	As an aid in the prevention of bacterial enteritis, also known as scours, baby pig diarrhea, vibrio dysentery, bloody dysentery, and salmonellosis (necro or necrotic enteritis).
Do	do	do	100 g/ton.	As an aid in the treatment of bacterial enteritis, also known as scours, baby pig diarrhea, vibrio dysentery, bloody dysentery, and salmonellosis (necro or necrotic enteritis).
Do	do	do	50 to 150 g/ton.	As an aid in the maintenance of weight gains and feed consumption in presence of atrophic rhinitis.

Drug sponsor	Type A article	Species	Use levels	Indications for use
Do.....	do.....	do.....	500 g/ton.....	In presence of porcine aplasia reduces intra- uterine abortion, gives higher birth rate, heavier and healthy new born pigs, reduces mortality shedding of leptospirosis and aids in maintaining normal weight gain and feed consumption. For 14 days, approximately month before farrowing. To increase rate of gain improve feed efficiency.
Do.....	do.....	Calves.....	0.05 to 0.1 mg/lb of body weight daily or 25 to 75 mg per head daily.	
Do.....	do.....	do.....	0.5 mg/lb of body weight daily or in complete feed at 50 g/ ton.	As an aid in the prevention of bacterial diarrhea.
Do.....	do.....	do.....	0.5 to 5.0 mg/lb of body weight daily or complete feed at 50 g/ton.	As an aid in the treatment of bacterial diarrhea.
Do.....	do.....	Cattle.....	75 to 80 mg per head daily..	As an aid in reducing incidence and severity of bacterial diarrhea. As an aid in reducing incidence and severity of abscesses (for cattle weighing over 400 lb). To increase rate of gain and improve feed efficiency. As an aid in increasing milk production lactating dairy cows.
Do.....	do.....	do.....	0.1 to 0.5 mg/lb of body weight daily.	As an aid in the prevention of bacterial diarrhea.
Do.....	do.....	do.....	0.5 to 5.0 mg/lb of body weight daily.	As an aid in the treatment of bacterial diarrhea, known as scours.
Do.....	do.....	do.....	0.5 to 2.0 g per head daily.	For the prevention and treatment of the early stages of shipping fever complex. Oxy- tetracycline is effective prophylaxis when fed 3 to 5 days preceding shipment and/or 3 to 5 days following arrival in feed-lots. For treatment of shipping fever these levels should be fed until onset of the disease symptoms disappear.
Pfizer, Inc.....	Oxytetracycline.....	Sheep.....	10 to 20 g/ton.....	To increase rate of gain and improve feed efficiency during finishing period.
Do.....	do.....	do.....	50 g/ton.....	As an aid in the prevention of bacterial diarrhea, also known as scours, lamb dysentery, and white scours in lambs.
Do.....	do.....	do.....	100 g/ton.....	As an aid in the treatment of bacterial diarrhea, also known as scours, lamb dysentery, and white scours in lambs.
Do.....	do.....	do.....	25 mg per head daily.	As an aid in reduction of losses due to enterotoxemia, also known as overeating disease.

Drug sponsor	Type A article	Species	Use levels	Indications for use
Do	Penicillin and streptomycin	Chickens, turkeys, and swine	Secs. 510.515 and 558.460	Secs. 510.515 and 558.460
American Cyanamid Co.	Chlortetracycline and sulfamethazine	Cattle	Sec. 558.128	Sec. 558.128
Mark Sharp & Dohme Research Labs.	Procaine penicillin and streptomycin sulfate	Sec. 558.460	Sec. 558.460	Sec. 558.460
CEVA Laboratories, Inc.	Erythromycin	Cattle	37 mg per head per day	Sec. 558.248
Hoffman-La Roche, Inc.	Sulfadimethoxine and ometoprim	Chickens and turkeys	Sec. 558.575	Sec. 558.575
Pfizer, Inc.	Oxytetracycline	Chickens	10 to 50 g/ton	As an aid in increasing egg production.
Do	do	do	50 to 100 g/ton	To extend period of high egg production, to improve feed efficiency, to improve fertility, and to improve egg production and feed efficiency in presence of disease and at time of stress; as an aid in maintaining and improving hatchability where birds are suffering stress from moving, vaccination, culling, extreme temperature change, and worming; to improve livability of progeny when losses are due to oxytetracycline-susceptible organisms; to improve egg shell quality.
Do	Oxytetracycline and neomycin	Chickens, turkeys, swine, and calves	As provided in paragraph (g)(2) of this section.	As provided in paragraph (g)(2) of this section.
American Cyanamid Co. and Pfizer, Inc.	Chlortetracycline, sulfamethazine, and penicillin	Swine	do	Do.
Farnam Animal Health Co.	Chlortetracycline, sulfathiazole, and penicillin	do	do	Do.
Hoe & Clark and SmithKline Animal Health Products	Furazolidone	Chickens and turkeys	0.00083 to 0.0011 percent (7½ to 10 g/ton)	To stimulate growth and improve feed efficiency of chickens and turkeys when fed continuously.
Do	do	do	0.0055 percent (50 g/ton)	For prevention of fowl typhoid, paratyphoid, and pullorum in chickens and turkeys when fed continuously in birds older than 2 weeks of age. For aid in prevention of coccidiosis in chickens caused by <i>E. tenella</i> , <i>E. necatrix</i> , or <i>E. acervulina</i> when fed continuously.
Do	do	do	0.0055-0.011 percent (50-100 g/ton)	Aid in maintenance of feed consumption and growth and reduction of morbidity and mortality due to stress and the following nonspecific conditions. Chronic respiratory disease (air-sac), infectious sinusitis, synovitis (arthritis due to a filterable agent), nonspecific enteritis (bluecomb, mud fever) and quail disease (ulcerative enteritis) when fed continuously prior to or throughout the danger period and during times of stress.

Drug sponsor	Type A article	Species	Use level	Indications for use
Do.	do	do	0.011 percent (100 g/ton).	For prevention of fowl typhoid, paratyphoid and pullorum in chickens and turkeys when fed for the first 2 weeks of the birds' life and followed continuously thereafter by this level (i.e., 0.0065 percent). For treatment of typhoid, paratyphoid, and pullorum in chickens and turkeys when fed for at least 2 weeks except when paratyphoid is due to <i>S. typhimurium</i> .
Do.	do	do	do	For reduction of conditions due to chronic respiratory disease air-sac complex associated with vaccination stress, feed continuously beginning at least 1 week before vaccination. For prevention of infectious hepatitis when fed continuously during the danger period. For control of coccidiosis in chickens caused by <i>E. tenella</i> , <i>E. necatrix</i> or <i>E. acroovum</i> when fed for 5 to 7 days longer and followed by this level (i.e., 0.0065 percent) for 2 weeks to aid in preventing recurrence.
Do.	do	do	do	For prevention of bacillary (histomoniasis, enteroperitonitis) in chickens and turkeys when fed continuously. For prevention of paratyphoid in chickens and turkeys when fed throughout the danger period. For control of chronic respiratory disease (air-sac), infectious sinusitis, synovitis (arthritis due to a filterable agent), nonspecific enteritis (bluecomb, mud fever) or quail disease (ulcerative enteritis) when fed for 5 to 10 days and followed with this level (i.e., 0.0065 percent) to aid in preventing recurrence. (NOTE.—Severe outbreaks may require twice the level specified; i.e., 0.013 percent).
Do.	do	do	0.011 to 0.022 percent (100 to 200 g/ton).	Aid in maintenance of bird consumption and growth and reduction of mortality and morbidity due to lesions for the control of the following nonspecific conditions: Chronic respiratory disease (air-sac), infectious sinusitis, synovitis (arthritis due to a filterable agent), nonspecific enteritis (bluecomb, mud fever), and quail disease (ulcerative enteritis) when fed 5 to 10 days. Follow with preventive level to prevent recurrence.

Drug sponsor	Type A article	Species	Use levels	Indications for use
Do.....	do.....	do.....	0.022 percent (200 g/ton).	For treatment of paratyphoid due to <i>S. typhimurium</i> when fed for 2 weeks. For treatment of blackhead (histomoniasis enterohepatitis) in chickens and turkeys when fed for 2 to 3 weeks (following diagnosis). For treatment of paracolon in chickens and turkeys and hexamitiasis in turkeys when fed for 2 weeks or longer (following diagnosis). For control of chronic respiratory disease (air-sac), infectious sinusitis, synovitis (arthritis due to a filterable agent), nonspecific enteritis (bluecomb, mud fever), and quail disease (ulcerative enteritis; when fed for 5 to 10 days and followed with 1/4 this level (i.e., 0.0055 percent) to aid in preventing recurrences. For treatment of infectious hepatitis in chickens when fed for 14 days and repeated as necessary.
Do.....	do.....	Swine.....	Sec. 558.262	Sec. 558.262.
Do.....	Nitrofurazone.....	Chickens.....	0.0055 percent (50 g/ton).	Aid in prevention of coccidiosis when fed continuously.
Do.....	do.....	Turkeys.....	do.....	As an aid in controlling losses due to secondary bacterial invasions concurrent with coccidiosis outbreaks when fed continuously throughout the danger period.
Do.....	do.....	Swine.....	0.055 percent (500 g/ton).	Treatment of necrotic enteritis caused by <i>S. choleraesuis</i> .

(2) The following is a list of drug combinations permitted when prepared from antibacterial Type A articles listed in paragraph (g)(1) of this section. Drug combinations listed in Subpart B of this part name their sponsors and are incorporated herein by reference since they are safe and effective by contemporary standards, or such sponsors have been notified of any additional safety or efficacy data required on an individual basis:

Drug sponsor	Type A article	Species	Use levels	Indications for use
Farnam Animal Health Co.....	Chlortetracycline and arsenic acid.	Swine.....	10 to 50 g/ton and 0.005 to 0.01 percent.	Enhancement of growth and feed efficiency.
American Cyanamid Co.....	Chlortetracycline and sulfamethazine.	Cattle.....	Sec. 558.128	Sec. 558.128.
Pfizer, Inc., and VPO, Inc.....	Oxytetracycline and neomycin base.	Chickens.....	50 g/ton and 35 to 140 g/ton.	Prevention of diseases from oxytetracycline susceptible organisms during periods of stress. As an aid in the prevention of bacterial enteritis and in the control of neomycin-sensitive organisms associated with bluecomb (mud fever or nonspecific enteritis).

Drug sponsor	Type A article	Species	Use levels	Indications for use
Do.....	do.....	Chickens (first 2 weeks).	50 to 100 g/ton and 35 to 140 g/ton.	Prevention of early chick mortality due to oxytetracycline-susceptible organisms, an aid in the prevention of bacterial enteritis and in the control of neomycin-sensitive organisms associated with bluecomb (mud fever or nonspecific enteritis).
Do.....	do.....	Chickens.	do.....	To extend period of high production, to improve efficiency, to improve production and feed efficiency in presence of disease and at time of stress. As an aid in maintaining and improving hatchability when birds are suffering stress from moving, vaccination, culling, extreme temperature changes, and worming; improve livability of progeny when losses are due to oxytetracycline-susceptible organisms, to improve egg quality, prevention of bluecomb (mud fever or nonspecific enteritis). As an aid in the prevention of bacterial enteritis and in the control of neomycin-sensitive organisms associated with bluecomb (mud fever or nonspecific enteritis).
Do.....	do.....	do.....	100 to 200 g/ton and 35 to 140 g/ton.	Prevention of complicated chronic respiratory disease (air-sac infection) and control of complicated chronic respiratory disease by lowering mortality and severity during outbreaks. As an aid in the prevention of bacterial enteritis and in the control of neomycin-sensitive organisms associated with bluecomb (mud fever or nonspecific enteritis).
Pfizer, Inc.	do.....	Turkeys.	50 g/ton and 35 to 140 g/ton.	As an aid in the prevention of disease from oxytetracycline-susceptible organisms during periods of stress. As an aid in the prevention of bacterial enteritis and in the control of neomycin-sensitive organisms associated with bluecomb (mud fever or nonspecific enteritis).

Drug sponsor	Type A article	Species	Use levels	Indications for use
Do	do	do	50 to 100 g/ton and 35 to 140 g/ton.	To extend period of high egg production, to improve egg production, to improve feed efficiency, to improve fertility, to improve egg production and feed efficiency in presence of disease and time of stress; as an aid in maintaining and improving hatchability where birds are suffering from stress, exposure, moving, vaccination, culling, extreme losses due to oxytetracycline-susceptible organisms, and to improve egg shell quality prevention of hexamitiasis. As an aid in the prevention of bacterial enteritis and in the control of neomycin-sensitive organisms associated with bluecomb (mud fever or nonspecific enteritis).
Do	do	Turkeys (first 4 weeks).	do	As an aid in the prevention of early poult mortality due to oxytetracycline-susceptible organisms. As an aid in the prevention of bacterial enteritis and in the control of neomycin-sensitive organisms associated with bluecomb (mud fever or nonspecific enteritis).
Do	do	do	100 to 150 g/ton and 35 to 100 g/ton.	As an aid in reducing mortality in birds which have suffered an attack of air-sacculitis (it is recommended, wherever possible, to feed from time of attack to marketing).
Do	do	Turkeys	do	As an aid in the prevention of bacterial enteritis and in the control of neomycin-sensitive organisms associated with bluecomb (mud fever or nonspecific enteritis).
Do	do	do	100 to 200 g/ton and 35 to 140 g/ton.	Control of bluecomb (mud fever or nonspecific enteritis), infectious sinusitis and hexamitiasis, prevention of infectious synovitis. As an aid in the prevention of bacterial enteritis and in the control of neomycin-sensitive organisms associated with bluecomb (mud fever or nonspecific enteritis).
Do	do	do	200 g/ton and 70 to 140 g/ton.	Control of infectious synovitis. For the treatment of bacterial enteritis and bluecomb (mud fever or nonspecific enteritis).
Pittman, Inc., and VPO, Inc.	do	Swine	50 g/ton and 35 to 140 g/ton.	As an aid in the prevention of bacterial enteritis (scours), baby pig diarrhea (in baby pigs only), vibronic dysentery, bloody dysentery, and salmonellosis (necro or necrotic enteritis).

Drug sponsor	Type A article	Species	Use levels	Indications for use
Do.....	do.....	do.....	50 to 150 g/ton and 70 to 140 g/ton.	As an aid in the maintenance of weight gains and for consumption in the presence of atrophic rhinitis. As an aid in the treatment of bacterial enteritis.
Pfizer, Inc.....	do.....	Calves.....	50 g/ton and 35 to 140 g/ton.	As an aid in the prevention of bacterial enteritis (scours).
Do.....	do.....	do.....	100 g/ton and 70 to 140 g/ton.	As an aid in the treatment of bacterial enteritis (scours).
Do.....	do.....	do.....	8 to 100 mg/gal and 100 to 200 mg/gal reconstituted milk replacer.	As an aid in the prevention of bacterial diarrhea (scours).
Do.....	do.....	do.....	40 to 200 mg/gal and 200 to 400 mg/gal reconstituted milk replacer.	As an aid in the treatment of bacterial diarrhea (scours).
The Upjohn Co.....	Lincomycin, amprolium, and ethopabate.	Chickens.....	Secs. 558.58 and 558.525.	Secs. 558.58 and 558.325.
Do.....	Lincomycin and zoalene.	do.....	Secs. 558.325 and 558.680.	Secs. 558.325 and 558.680.
Do.....	Lincomycin, amprolium, ethopabate, and roxarsone.	do.....	Secs. 558.58, 558.325, and 558.530.	Secs. 558.58, 558.325, and 558.530.
Do.....	Lincomycin, monensin, and roxarsone.	do.....	Secs. 558.325, 558.355, and 558.530.	Secs. 558.325, 558.355, and 558.530.
Merck Sharp & Dohme Research Labs, and Pfizer, Inc.	Procaine penicillin and streptomycin.	Chickens and turkeys.	2.4 to 7.5 g/ton and 12.0 to 37.5 g/ton.	Sec. 558.460.
Do.....	do.....	do.....	3.75 to 7.5 g/ton and 18.75 to 37.5 g/ton.	Do.
Do.....	do.....	Chickens.....	3.75 to 30 g/ton and 18.75 to 150 g/ton.	Do.
Do.....	do.....	Turkeys.....	15 to 30 g/ton and 75 to 150 g/ton.	Do.
Do.....	do.....	Chickens.....	2.4 to 25 g/ton and 15 to 75 g/ton.	Sec. 510.515.
Do.....	do.....	Swine.....	1.5 to 7.5 g/ton and 7.5 to 37.5 g/ton.	Sec. 558.460.
Do.....	do.....	do.....	7.5 to 45 g/ton and 37.5 to 225 g/ton.	Do.
Do.....	do.....	do.....	5 to 25 g/ton and 15 to 75 g/ton.	Sec. 510.515.
Do.....	Procaine penicillin, streptomycin, and arsenic acid.	do.....	1.5 to 7.5 g/ton, 7.5 to 37.5 g/ton, and 45 to 90 g/ton.	Do.
Do.....	Nicarbazin and procaine penicillin.	Chickens.....	0.01 to 0.02 percent and 2.4 to 50 g/ton.	Do.
Do.....	Nicarbazin and bacitracin methylene disalicylate.	do.....	0.01 to 0.02 percent and 4 to 50 g/ton.	Do.
Do.....	Nicarbazin, bacitracin methylene disalicylate, and roxarsone.	do.....	0.01 to 0.02 percent, 4 to 50 g/ton, and 0.0025 to 0.005 percent.	Do.

Drug sponsor	Type A article	Species	Use levels	Indications for use
Do	Nicarbazin, procaine penicillin, and roxarsone.	do	0.01 to 0.02 percent, 2.4 to 50 g/ton, and 0.0025 to 0.025 percent.	Do.
Do	Amprolium and bacitracin methylene disalicylate.	Chickens and turkeys.	0.0125 to 0.025 percent and 4 to 50 g/ton.	Secs. 558.55 and 558.76.
Do	Amprolium, ethopabate, and bacitracin methylene disalicylate.	Chickens.	0.0125 to 0.025 percent, 0.0004 percent, and 4 to 50 g/ton.	Secs. 558.58 and 558.76.
Do	Amprolium, ethopabate, bacitracin methylene disalicylate, and roxarsone.	do	0.0125 to 0.025 percent, 0.0004 percent, 4 to 50 g/ton, and 0.0025 to 0.005 percent.	Secs. 558.58, 558.76, and 558.530.
Do	Amprolium and procaine penicillin.	Chickens and turkeys.	0.004 to 0.025 percent and 2.4 to 50 g/ton.	Secs. 558.55 and 558.460.
Do	Amprolium, procaine penicillin, and roxarsone.	Chickens.	0.004 to 0.025 percent, 2.4 to 50 g/ton, and 0.0025 to 0.005 percent.	Secs. 558.55, 558.460, and 558.530.
Do	Amprolium, ethopabate, procaine penicillin, and erythromycin.	do	0.0125 to 0.025 percent, 0.0004 percent, 2.4 to 50 g/ton, and 4.6 to 18.5 g/ton.	Secs. 558.58 and 558.460.
Do	Amprolium and erythromycin.	do	0.0125 to 0.025 percent and 4.6 to 18.5 g/ton.	Sec. 558.55.
Do	Amprolium and ethopabate.	do	0.0125 to 0.025 percent and 0.0004 percent.	Sec. 558-58.
Do	Amprolium, arsenic acid, and erythromycin.	do	0.0125 to 0.025 percent, 0.01 percent, and 4.6 to 18.5 g/ton.	Sec. 558.55.
Do	Amprolium, arsenic acid, and ethopabate.	do	0.0125 to 0.025 percent, 0.01 percent, and 0.0004 percent.	Sec. 558.58.
Do	Amprolium, ethopabate, and bacitracin methylene disalicylate.	do	0.0125 percent, 0.004 percent, and 4 to 50 g/ton.	Do.
Do	Amprolium, ethopabate, bacitracin methylene disalicylate, and roxarsone.	do	0.0125 percent, 0.004 percent, 5 to 35 g/ton, and 0.00375 percent.	Do.
van-Moore, Inc.	Bacitracin zinc, amprolium, and ethopabate.	do	4 to 50 g/ton, 0.0125 to 0.025 percent, and 0.0004 percent.	Prevention of coccidiosis. Growth promotion and feed efficiency. Sec. 558.78.
Do	Bacitracin zinc, amprolium, ethopabate, and roxarsone.	do	4 to 50 g/ton, 0.0125 to 0.025 percent, 0.0004 percent, and 0.0025 to 0.005 percent.	Prevention of coccidiosis. Growth promotion and feed efficiency. Improving pigmentation. Sec. 558.78.
Do	Bacitracin zinc and arsenic acid.	Swine	10 to 50 g/ton and 0.005 to 0.01 percent.	Increased rate of weight gain and improved feed efficiency.

Drug sponsor	Type A article	Species	Use levels	Indications for use
Merck Sharp & Dohme Research Labs.	Amprolium, ethopabate, procaine penicillin, and roxarsone.	Chickens.....	0.125 to 0.025 percent, 0.0004 percent, 2.4 to 50 g/ton, and 0.0025 to 0.005 percent.	Secs. 558.58, 558.480 and 558.530.
Pfizer, Inc.	Penicillin and streptomycin.	Chickens and turkeys.....	2.4 to 25 g/ton and 15 to 75 g/ton.	Sec. 510.515.
Do.....	Penicillin and streptomycin.	Swine.....	5 to 25 g/ton and 15 to 75 g/ton.	Do.
Dow Chemical Co.	Zoalene and bacitracin methylene disalcylate.	Chickens.....	0.0125 percent and 4 to 50 g/ton.	Sec. 558.680.
Do.....	Zoalene, roxarsone, and bacitracin methylene disalcylate.	do.....	0.0125 percent, 0.005 percent, and 4 to 50 g/ton.	Do.
Do.....	Zoalene and bacitracin zinc.	do.....	0.0125 percent and 4 to 50 g/ton.	Do.
Do.....	Zoalene, roxarsone, and bacitracin zinc.	do.....	0.0125 percent, 0.0025 to 0.005 percent, and 4 to 50 g/ton.	Do.
Do.....	Zoalene and penicillin.	do.....	0.0125 percent and 2.4 to 50 g/ton.	Do.
Do.....	Zoalene, roxarsone, and penicillin.	do.....	0.0125 percent, 0.0025 to 0.005 percent, and 2.4 to 50 g/ton.	Do.
Do.....	Zoalene, arsenic acid, and bacitracin methylene disalcylate or bacitracin zinc.	do.....	0.0125 percent, 0.01 percent, and 4 to 50 g/ton.	Do.
Do.....	Zoalene, arsenic acid, and penicillin.	do.....	0.0125 percent, 0.01 percent, and 2.4 to 50 g/ton.	Do.
Do.....	Zoalene, and bacitracin methylene disalcylate.	do.....	0.004 to 0.0125 percent and 4 to 50 g/ton.	Do.
Do.....	Zoalene, roxarsone, and bacitracin methylene disalcylate.	do.....	0.004 to 0.0125 percent, 0.0025 to 0.005 percent, and 4 to 50 g/ton.	Do.
Hess & Clark and SmithKline Animal Health Products.	Furazolidone and oxytetracycline.	Swine.....	0.022 percent (200 g/ton) and 50 to 150 g/ton.	Prevention of bacterial enteritis (necrotic enteritis, necrotic and vibronic (bloody) dysentery; growth promotion while on medication when fed to prestarters, starters, and growing rations to baby pig and growing swine for 1 weeks. As an aid in the maintenance of weight gain and feed consumption in presence of atrophic rhinitis.

Drug sponsor	Type A article	Species	Use levels	Indications for use
Do.....	Furazolidone, oxytetracycline, and arsenic acid.	do.....	0.011 percent (100 g/ton), 50 to 100 g/ton, and 0.005 to 0.01 percent.	Prevention of bacterial enteritis (necrotic enteritis, necro) and vibronic (bloody) dysentery; growth promotion while on medication and when fed in prestarters, starters, and growing rations to baby pigs and growing swine for 5 weeks. As an aid in the maintenance of weight gains and feed consumption in presence of atrophic rhinitis. Growth promotion and feed efficiency.
Do.....	Furazolidone and bacitracin methylene disalicylate, bacitracin zinc, or procaine penicillin.	Chickens and turkeys.	0.011 to 0.022 percent (100 to 200 g/ton) and 4 to 50 g/ton, or 2.4 to 50 g/ton.	Sec. 510.515.
Do.....	Furazolidone and oxytetracycline.	Swine.....	0.011 percent (100 g/ton) and 50 to 150 g/ton.	Prevention of bacterial enteritis (necrotic enteritis, necro) and vibronic (bloody) dysentery; growth promotion while on medication and when fed in prestarters, starters, and growing swine for 5 weeks. As an aid in the maintenance of weight gains and feed consumption in presence of atrophic rhinitis.
Do.....	do.....	do.....	0.0165 percent (150 g/ton) and 50 to 150 g/ton.	Prevention of bacterial enteritis (necrotic enteritis, necro) and vibronic (bloody) dysentery; growth promotion while on medication and when fed in prestarters, starters, and growing swine for 3 weeks. As an aid in the maintenance of weight gains and feed consumption in presence of atrophic rhinitis.
Do.....	Furazolidone, oxytetracycline, and arsenic acid.	do.....	0.0165 percent (150 g/ton), 50 to 100 g/ton, and 0.005 to 0.01 percent.	Prevention of bacterial enteritis (necrotic enteritis, necro) and vibronic (bloody) dysentery; growth promotion while on medication when fed in prestarters, starters, and growing rations to baby pigs and growing swine for 3 weeks. As an aid in the maintenance of weight gains and feed consumption in presence of atrophic rhinitis. Growth promotion and feed efficiency.
Do.....	do.....	do.....	0.022 percent, 50 to 100 g/ton, and 0.005 to 0.01 percent.	Prevention of bacterial enteritis (necrotic enteritis, necro) and vibronic (bloody) dysentery; growth promotion while on medication when fed in prestarters, starters, and growing rations to baby pigs and growing swine for 2 weeks. As an aid in the maintenance of weight gains and feed consumption in presence of atrophic rhinitis. Growth promotion and feed efficiency.
Mayer Labs, Inc.....	Carbarsone and bacitracin.	Turkeys.....	Sec. 558.120.....	Sec. 558.120.

Drug sponsor	Type A article	Species	Use levels	Indications for use
Elanco Products Co.	Hygromycin B and tylosin.	Chickens.	6 to 12 g/ton and 4 to 50 g/ton.	Sec. 558.274.
Do.	do.	Swine.	12 g/ton and 10 to 100 g/ton.	Do.
Salisbury Laboratories.	Nitarsone and bacitracin zinc.	Turkeys.	0.01875 percent, 4 to 50 g/ton.	As an aid in the prevention of blackhead. To increase weight gain and improve feed efficiency.

[51 FR 8811, Mar. 14, 1986; 51 FR 11014, Apr. 1, 1986, as amended at 51 FR 28547, Aug. 1986; 53 FR 20843, June 7, 1988]

§ 558.20 Drugs used in medicated feeds in use before January 1, 1958, which are not otherwise listed; interim listing.

Applications for animal feeds bearing or containing new animal drugs shall contain a reference to a section in the new animal drug regulations where the drug and the intended use are listed. For the purposes of such applications the following list identifies drugs that are required to be the subject of approved medicated feed applications for the indicated uses which are not listed in other new animal drug regulations. The drugs are not listed elsewhere for these uses in other new animal drug regulations because they were so used prior to the Food Additives Amendment of 1958 which required the listing of such drugs in appropriate regulations.

Drug ingredient	Species	Use levels	Indications for use	Limitations
Arsanilate sodium.	Swine.	0.005 to 0.01%.	Increase rate of gain and improve feed efficiency in growing swine.	Withdraw 5 days before slaughter. As sole source of organic arsenic.
Do.	do.	0.01%.	Control of swine dysentery (hemorrhagic enteritis, bloody dysentery).	Withdraw 5 days before slaughter. Feed continuously as sole source of organic arsenic.
Do.	do.	0.025 to 0.04%.	Treatment of swine dysentery (hemorrhagic enteritis, bloody dysentery).	Withdraw 5 days before slaughter. Feed for 5-6 days as sole source of organic arsenic.
Arsanilic acid.	do.	0.005 to 0.01%.	Increase rate of gain and improve feed efficiency in growing swine.	Withdraw 5 days before slaughter. As sole source of organic arsenic.
Do.	do.	0.01%.	Control of swine dysentery (hemorrhagic enteritis, bloody dysentery).	Withdraw 5 days before slaughter. Feed continuously as sole source of organic arsenic.
Do.	do.	0.025 to 0.04%.	Treatment of swine dysentery (hemorrhagic enteritis, bloody dysentery).	Withdraw 5 days before slaughter. Feed for 5-6 days as sole source of organic arsenic.
Butynorate (dibutyltin dilaurate).	Turkeys.	0.0375%.	As an aid in the prevention of coccidiosis (caused by <i>E. meleagridis</i> , <i>E. meleagris</i> , <i>E. gallipavonis</i>) and hexamitiasis.	Withdraw 7 days before slaughter.
Neomycin sulfate.	Chickens, turkeys, and ducks.	70 to 140 g/ton of complete feed as neomycin base.	For treatment of bacterial enteritis (nonspecific enteritis, salmonellosis, bluecomb, mud fever).	Withdrawal before slaughter: 30 days, cattle; 20 days, sheep and swine; 14 days, turkeys, ducks, and laying hens; 5 days, broiler chickens.
Do.	Mink.	140 g/ton of complete feed as neomycin base.	For treatment of bacterial enteritis and diarrhea.	Do.

Drug ingredient	Species	Use levels	Indications for use	Limitations
Do	Swine, calves, cattle, horses, sheep, goats.	70 to 140 g/ton of complete feed as neomycin base.	For treatment of bacterial enteritis (scours, diarrhea, bloody dysentery, vibronic dysentery, winter dysentery, white scours, coli-bacillosis, salmonellosis, diarrhea caused by <i>E. coli</i> vibrio and salmonella organisms); enterotoxemia in lambs.	Do.
Nitrophenyl-arsinic acid, Phenothiazine	Chickens and turkeys.	0.01875%	As an aid in the prevention of blackhead.	Withdraw 5 days before slaughter. As sole source of organic arsenic.
Do	Chickens	0.5 g per bird.	Removal of cecal worms (<i>Haemonchus</i> spp.).	For 1 day only.
Do	Turkeys	1 g per bird.	do.	Do.
Do	Swine	5 g up to 25 lb; 8 g, 26 to 50 lb; 10 g, 51 to 100 lb; 20 g, 101 to 200 lb; 30 g, 201 lb and up.	Removes nodular worms (<i>Oesophagostomum</i>).	Do.
Do	Sheep and goats.	20 to 60 lb body weight, 12.5 g; over 60 lb body weight, 25 g.	Removal of stomach worms (<i>Haemonchus</i> , <i>Ostertagia</i> , and <i>Trichostrongylus</i> spp.); large-mouth bowel worms (<i>Chabertia</i> spp.), and hookworms (<i>Bunostomum</i> spp.).	Milk from dairy animals which have been treated with phenothiazine should not be used for food for 4 days following treatment.
Do	do	1g/head/day	Control of stomach worms (<i>Haemonchus</i> , <i>Ostertagia</i> , and <i>Trichostrongylus</i> spp.); large-mouth bowel worms and hookworms (<i>Chabertia</i> spp.), (<i>Bunostomum</i> spp.).	Do not feed to lactating dairy animals. Feed continuously.
Do	Cattle	10 g/100 lb body weight, up to a maximum of 70 g.	Removes common stomach worms (<i>Haemonchus</i>), lesser stomach worms (<i>Ostertagia</i>), hair worms, bankrupt worms (<i>Trichostrongylus</i> spp.), nodular worm (<i>Oesophagostomum</i> spp.), and large-mouth bowel worms (<i>Chabertia</i> spp.).	Milk from dairy animals which have been treated with phenothiazine should not be used for food for 4 days following treatment.
Do	do	20 g/100 lb body weight up to a maximum of 80 g. Micronized (2-3 micron size particles)—10 g/100 lb body weight, up to a maximum of 60 g.	Hookworms (<i>Bunostomum</i> spp.).	For 1 day only. Milk from dairy animals which have been treated with phenothiazine should not be used for food for 4 days following treatment.
Do	do	0.25 g/100 lb body weight/day. For adult average dose is 2 g.	Controls common stomach worms (<i>Haemonchus</i>), lesser stomach worms (<i>Ostertagia</i>), hair worms, bankrupt worms (<i>Trichostrongylus</i> spp.), nodular worm (<i>Oesophagostomum</i> spp.), and large-mouth bowel worms (<i>Chabertia</i> spp.).	Do not feed to lactating dairy animals.
Do	Horses and mules.	2.5 g/100 lb body weight up to a maximum of 30 g.	Removal of strongyles (<i>Strongylus</i> spp.).	For 1 day only.
Do	do	2 g per head per day	do	For continuous use; feed 2 g per head per day for 21 consecutive days then none for 9 days. Repeat the feeding schedule as long as worm control is desired.

Drug ingredient	Species	Use levels	Indications for use	Limitations
Piperazine	Chickens (under 6 weeks of age).	0.2 to 0.4%	Control of infestation of large roundworms (<i>Ascaris</i>).	As sole source of feed, day treatment. Directions use should assure the amount of feed consumed will furnish in 1 day 100 mg of piperazine per bird.
Do	Chickens (over 6 weeks of age).	do	do	As sole source of feed, day treatment. Directions use should assure the amount of feed consumed will furnish in 1 day 100 mg of piperazine per bird.
Do	Turkeys (under 12 weeks of age).	do	do	As sole source of feed, day treatment. Directions use should assure the amount of feed consumed will furnish in 1 day 100 mg of piperazine per bird.
Do	Turkeys (over 12 weeks of age).	do	do	As sole source of feed, day treatment. Directions use should assure the amount of feed consumed will furnish in 1 day 100 mg of piperazine per bird according to size.

[51 FR 7394, Mar. 3, 1986]

Subpart B—Specific New Animal Drugs for Use in Animal Feeds

§ 558.35 Aklomide.

(a) **Approvals.** Type A medicated articles: to 017210 in § 510.600(c) of this chapter, as follows:

- (1) 50 percent aklomide.
- (2) 20 percent sulfanitrin and 25 percent aklomide.
- (3) 25 percent aklomide, 20 percent sulfanitrin, and 5 percent roxarsone.
- (4) 50 percent aklomide and 10 percent roxarsone.

(b) **Related tolerances.** See § 556.30 of this chapter.

(c) **Conditions of use.** It is used in feed for chickens as follows:

(1) **Amount per ton.** Aklomide, 227 grams (0.025 percent).

(i) **Indications for use.** As an aid in the prevention of coccidiosis caused by *E. tenella* and *E. necatrix*.

(ii) **Limitations.** Not to be fed to birds laying eggs for human consumption.

(2) **Amount per ton.** Aklomide, 227 grams (0.025 percent) combined with sulfanitrin, 181.6 grams (0.02 percent).

(i) **Indications for use.** As an aid in the prevention of coccidiosis caused by

E. tenella, *E. necatrix*, and *E. acervulina*.

(ii) **Limitations.** Not to be fed laying chickens; withdraw 5 days before slaughter.

(3) **Amount per ton.** Aklomide, 227 grams (0.025 percent) combined with sulfanitrin, 181.6 grams (0.02 percent) + roxarsone, 22.7-45.4 grams (0.0025-0.005 percent).

(i) **Indications for use.** As an aid in the prevention of coccidiosis caused by *E. tenella*, *E. necatrix*, and *E. acervulina*; growth promotion and feed efficiency; improving pigmentation.

(ii) **Limitations.** Not to be fed laying chickens; withdraw 5 days before slaughter; as sole source of organic arsenic; chickens should have access to drinking water at all times.

(4) **Amount per ton.** Aklomide, 227 grams (0.025 percent) combined with roxarsone, 22.7-45.4 grams (0.0025-0.005 percent).

(i) **Indications for use.** As an aid in the prevention of coccidiosis caused by *E. tenella*, and *E. necatrix*; growth promotion and feed efficiency; improving pigmentation.

(ii) **Limitations.** Not to be fed to birds laying eggs for human consumption; withdraw 5 days before slaughter; as sole source of organic arsenic.

chickens should have access to drinking water at all times.

(40 FR 13959, Mar. 27, 1975, as amended at 41 FR 6312, Feb. 25, 1976; 51 FR 7395, Mar. 2, 1986)

§ 558.55 Amprolium.

(a) *Approvals.* Type A medicated articles: 25 percent to 000006 in § 510.000(c) of this chapter for use as in paragraph (d) of this section.

(b) *Special considerations.* Do not use in Type B or Type C medicated feeds containing bentonite.

(c) *Related tolerances.* See § 556.50 of this chapter.

(d) *Conditions of use—(1) Calves.* It is top-dressed on or thoroughly mixed in the daily feed ration as follows:

(i) *Amount.* 227 milligrams per 100 pounds (5 milligrams per kilogram) body weight per day.

(a) *Indications for use.* As an aid in the prevention of coccidiosis caused by *Eimeria bovis* and *E. zurnii*.

(b) *Limitations.* Administer from a Type B feed containing from 0.05 to

1.25 percent amprolium with the usual amount of feed consumed in 1 day; feed for 21 days during periods of exposure or when experience indicates that coccidiosis is likely to be a hazard; withdraw 24 hours before slaughter; as sole source of amprolium.

(ii) *Amount.* 454 milligrams per 100 pounds (10 milligrams per kilogram) body weight per day.

(a) *Indications for use.* As an aid in the treatment of coccidiosis caused by *Eimeria bovis* and *E. zurnii*.

(b) *Limitations.* Administer from a Type B feed containing from 0.05 to 1.25 percent amprolium with the usual amount of feed consumed in 1 day; feed for 5 days; for a satisfactory diagnosis, a microscopic examination of the feces should be done by a veterinarian or diagnostic laboratory before treatment; when treating outbreaks, the drug should be administered promptly after diagnosis is determined; withdraw 24 hours before slaughter; as sole source of amprolium.

(2) *Chickens and turkeys.* It is used as follows:

Amprolium in grams per ton	Combination in grams per ton	Indications for use	Limitations
(i) 36.3 to 113.5 (0.004% to 0.0125%).		Replacement chickens; development of active immunity to coccidiosis.	Feed as follows—

Growing conditions	Up to 5 weeks of age	From 5 to 8 weeks of age	Over 8 weeks of age
	Amprolium grams per ton	Amprolium grams per ton	Amprolium grams per ton
Severe exposure to coccidiosis.	113.5 (0.0125%)	72.6-113.5 (0.008%—0.0125%)	36.3-113.5 (0.004%—0.0125%)
Moderate exposure to coccidiosis.	72.6-113.5 (0.008%—0.0125%)	54.5-113.5 (0.006%—0.0125%)	36.3-113.5 (0.004%—0.0125%)
Slight exposure to coccidiosis.	36.3-113.5 (0.004%—0.0125%)	36.3-113.5 (0.004%—0.0125%)	36.3-113.5 (0.004%—0.0125%)

Arsanilate sodium 90 (0.01%).	Replacement chickens; development of active immunity to coccidiosis; growth promotion and feed efficiency; improving pigmentation.	Withdraw 5 d before slaughter; as sole source of organic arsenic; feed according to subtable in item (i).
Arsanilic acid 90 (0.01%).	Replacement chickens; development of active immunity to coccidiosis; growth promotion and feed efficiency; improving pigmentation.	Withdraw 5 d before slaughter; as sole source of organic arsenic; feed according to subtable in item (i).
Arsanilic acid 90 (0.01%) plus erythromycin 4.6 to 18.5.	Replacement chickens; development of active immunity to coccidiosis; growth promotion and feed efficiency; improving pigmentation.	Withdraw 5 d before slaughter; as sole source of organic arsenic. Feed according to subtable in item (i).
Arsanilic acid 90 (0.01%) plus erythromycin 92.5.	1. Replacement chickens; development of active immunity to coccidiosis; growth promotion and feed efficiency; improving pigmentation; as an aid in the prevention of chronic respiratory disease during periods of stress. 2. Replacement chickens; development of active immunity to coccidiosis; growth promotion and feed efficiency; improving pigmentation; as an aid in the prevention of infectious coryza.	Feed for 2 d before stress and 3 to 6 d after stress; withdraw 5 d before slaughter; as sole source of organic arsenic. Feed according to subtable in item (i). Feed for 7 to 14 d; withdraw 5 d before slaughter; as sole source of organic arsenic. Feed according to subtable in item (i).

Amprolium in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
0.263 to 113.5 (0.004% to 0.0125%).	Ansanilic acid 90 (0.01%) plus erythromycin 185.	Replacement chickens; development of active immunity to coccidiosis; growth promotion and feed efficiency; improving pigmentation; as an aid in the prevention and reduction of lesions and in lowering severity of chronic respiratory disease.	Feed for 5 to 8 d; do not use in birds producing eggs for food purposes; withdraw 5 d before slaughter; as sole source of organic arsenic. Feed according to subtable in item (i).	
	Bacitracin 100 to 200...	Replacement chickens; development of active immunity to coccidiosis; treatment of chronic respiratory disease (air-sac infection) and blue comb (nonspecific infectious enteritis).	As bacitracin methylene disacrylate or bacitracin zinc. Feed according to subtable in item (i).	
	Chlortetracycline 100 to 200.	Replacement chickens; development of active immunity to coccidiosis; treatment of chronic respiratory disease (air-sac infection), blue comb (nonspecific infectious enteritis); prevention of synovitis.	Not to be fed to laying chickens; as chlortetracycline hydrochloride. Feed according to subtable in item (i).	
	Erythromycin 4.6 to 18.5.	Replacement chickens; development of active immunity to coccidiosis; growth promotion and feed efficiency.	As erythromycin thiocyanate. Feed according to subtable in item (i).	
	Erythromycin 82.5	1. Replacement chickens; development of active immunity to coccidiosis; as an aid in the prevention of infectious coryza. 2. Replacement chickens; development of active immunity to coccidiosis; as an aid in the prevention of chronic respiratory disease during periods of stress.	Feed for 7 to 14 d; withdraw 24 h before slaughter. Feed according to subtable in item (i). Feed for 2 d before stress and 3 to 6 d after stress; withdraw 24 h before slaughter. Feed according to subtable in item (i).	
	Erythromycin 185	Replacement chickens; development of active immunity to coccidiosis; as an aid in the prevention and reduction of lesions and in lowering severity of chronic respiratory disease.	Feed for 5 to 8 d; do not use in birds producing eggs for food purposes; withdraw 48 h before slaughter. Feed according to subtable in item (i).	
	Hygromycin B 8 to 12...	Replacement chickens; development of active immunity to coccidiosis; control of infestation of large round worms (<i>Ascaris galli</i>), cecal worms (<i>Heterakis gallinae</i>), and capillary worms (<i>Capillaria obelinate</i>).	Feed according to subtable in item (i).	
	Penicillin 2.4 to 50	Replacement chickens; development of active immunity to coccidiosis; growth promotion and feed efficiency.	As procaine penicillin. Feed according to subtable in item (i).	
	Penicillin plus streptomycin 90 to 180 (of combination).	Replacement chickens; development of active immunity to coccidiosis; treatment of chronic respiratory disease (air-sac infection), blue comb (nonspecific infectious enteritis).	Feed contains 16.7% penicillin; as procaine penicillin; as streptomycin sulfate. Feed according to subtable in item (i).	
	Roxarsone 22.7 to 45.4 (0.0025% to 0.005%).	Replacement chickens; development of active immunity to coccidiosis; growth promotion, and feed efficiency; improving pigmentation.	Withdraw 5 d before slaughter; as sole source of organic arsenic. Feed according to subtable in item (i).	

Amprolium in grams per ton	Combination in grams per ton	Indications for use	Limitations
(ii) 72.6 to 113.5 (0.008% to 0.0125%).		Broiler chickens; prevention of coccidiosis caused by <i>Eimeria tenella</i> only.	Withdraw 5 d before slaughter; as sole source of organic arsenic. Feed according to subtable in item (i).
	Arsanilate sodium 90 (0.01%).	Broiler chickens; prevention of coccidiosis caused by <i>E. tenella</i> only; growth promotion and feed efficiency; improving pigmentation.	Withdraw 5 d before slaughter; as sole source of organic arsenic.
	Arsanilic acid 90 (0.01%).	do	do
	Bacitracin 100 to 200	Broiler chickens; prevention of coccidiosis caused by <i>E. tenella</i> only; treatment of chronic respiratory disease (air-sac infection) and blue comb (nonspecific infectious enteritis).	As bacitracin methylene disulfoxide, or zinc bacitracin.
	Chlortetracycline 100 to 200.	Broiler chickens; prevention of coccidiosis caused by <i>E. tenella</i> only; treatment of chronic respiratory disease (air-sac infection), blue comb (nonspecific infectious enteritis); prevention of synovitis.	Not for laying chickens; as chlortetracycline hydrochloride.
	Hygromycin B 8 to 12	Broiler chickens; prevention of coccidiosis caused by <i>Eimeria tenella</i> only; control of infestation of large round worms (<i>Heterakis gallinae</i>) and capillary worms (<i>Capillaria obsoleta</i>).	Feed according to subtable in item (i).
	Penicillin 2.4 to 50	Broiler chickens; prevention of coccidiosis caused by <i>E. tenella</i> only; growth promotion and feed efficiency.	As procaine penicillin.
(iii) 113.5 (0.0125%)	Penicillin plus streptomycin 90 to 180 (of combination).	Treatment of chronic respiratory disease (air-sac infection), blue comb (nonspecific infectious enteritis).	Feed contains 16.7% penicillin; as procaine penicillin; as streptomycin sulfate.
	Roxarsone 22.7 to 45.4 (0.0025% to 0.005%).	Broiler chickens; prevention of coccidiosis caused by <i>E. tenella</i> only; growth promotion and feed efficiency; improving pigmentation.	Withdraw 5 d before slaughter; as sole source of organic arsenic.
		1. Laying chickens; prevention of coccidiosis. 2. Laying chickens; treatment of coccidiosis.	For moderate outbreaks of coccidiosis; administer for 2 weeks.
(iv) 113.5 to 227 (0.0125% to 0.025%).	Bambermycins 1 to 3 plus roxarsone 22.8 to 34.1 (0.0025% to 0.00375%).	Broiler chickens; as an aid in the prevention of coccidiosis; for increased rate of weight gain, improved feed efficiency, and improved pigmentation.	Feed continuously as the sole ration; as sole source of amprolium and organic arsenic; roxarsone as provided by No. 017210 in § 510.600(c) of this chapter, bambermycins by No. 012799; withdraw 5 d before slaughter.
	Bambermycins 1 to 4	Growing turkeys; prevention of coccidiosis; increased rate of weight gain and improved feed efficiency.	Feed continuously as the sole source of amprolium; bambermycins as provided by No. 012799 in § 510.600(c) of this chapter.
		1. Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis. 2. Turkeys; prevention of coccidiosis.	

Approval in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
(H) 113.5 to 227 (0.0125% to 0.025%).	Arsanilate sodium 90 (0.01%).	1. Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; growth promotion and feed efficiency; improving pigmentation. 2. Turkeys; prevention of coccidiosis; growth promotion and feed efficiency; improving pigmentation.	Withdraw 5 d before slaughter; as sole source of organic arsenic. do.....	012769
	Arsanilic acid 90 (0.01%).	1. Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; growth promotion and feed efficiency; improving pigmentation. 2. Turkeys; prevention of coccidiosis; growth promotion and feed efficiency; improving pigmentation.	do..... do.....	
	Arsanilic acid 90 (0.01%) plus erythromycin 92.5.	1. Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; growth promotion and feed efficiency; improving pigmentation; as an aid in the prevention of chronic respiratory disease during periods of stress. 2. Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; growth promotion and feed efficiency; improving pigmentation; as an aid in the prevention of infectious coryza.	Feed for 2 d before stress and 3 to 6 d after stress; withdraw 5 d before slaughter; as sole source of organic arsenic. Feed for 7 to 14 d; withdraw 5 d before slaughter; as sole source of organic arsenic.	
	Arsanilic acid 90 (0.01%) plus erythromycin 185.	Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; growth promotion and feed efficiency; improving pigmentation; as an aid in the prevention and reduction of lesions and in lowering severity of chronic respiratory disease.	Feed for 5 to 8 d; do not use in birds producing eggs for food purposes; withdraw 5 d before slaughter; as sole source of organic arsenic.	
	Arsanilic acid 90 (0.01%) plus erythromycin 4.6 to 18.5.	Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; growth promotion and feed efficiency; improved pigmentation.	Withdraw 5 d before slaughter; as sole source of organic arsenic.	
	Bacitracin 4 to 50.....	1. Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; growth promotion and feed efficiency. 2. Turkeys; prevention of coccidiosis; growth promotion and feed efficiency.	As bacitracin methylene disilicate or bacitracin zinc. do.....	

Amprolium in grams per ton	Combination in grams per ton	Indications for use	Limitations
(iv) 113.5 to 227 (0.0125% to 0.025%).	Bacitracin 100 to 200...	1. Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; treatment of chronic respiratory disease (air-sac infection), blue comb (non-specific infectious enteritis). 2. Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; treatment of chronic respiratory disease (air-sac infection), blue comb (non-specific infectious enteritis).	do As bacitracin zinc.....
	Bacitracin 100 to 500...	Turkeys; prevention of coccidiosis; treatment of infectious sinusitis, blue comb (mud fever).	As bacitracin zinc.....
	Bacitracin plus penicillin 100 to 500 (of combination).	do	Feed contains 50% to 75% of bacitracin but not more than 125 g penicillin; as procaine penicillin; as bacitracin zinc.
	Carbarsone 227 to 340.5.	Turkeys; aid in prevention of coccidiosis (<i>Eimeria adenocoides</i> , <i>E. meleagris</i> , and <i>E. gallipavonis</i>) and black-head.	Feed continuously 2 weeks before coccidiosis and black-head are expected and continue as long as prevention is needed; withdraw 5 days before slaughter; use as sole source of amprolium and organic arsenic; do not use as a treatment for outbreaks of coccidiosis; carbarsone by 011794 in § 510.600(c) of this chapter.
	Chlortetracycline 100 to 200.	Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; treatment of chronic respiratory disease (air-sac infection), blue comb (nonspecific infectious enteritis); prevention of synovitis.	Not for laying chickens, as chlortetracycline hydrochloride.
	Erythromycin ² 4.6 to 18.5.	Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; growth promotion and feed efficiency.	As erythromycin thiocyanate.....
	Erythromycin 92.5.....	1. Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; as an aid in the prevention of chronic respiratory disease during periods of stress. 2. Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; as an aid in the prevention of infectious coryza.	Feed for 2 d before stress and 3 to 6 d after stress; withdraw 24 h before slaughter. Feed for 7 to 14 d; withdraw 24 h before slaughter.

Amprolium in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
(b) 113.5 to 227 (0.0125% to 0.025%).	Erythromycin 185	Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; as an aid in the prevention and reduction of lesions and in lowering severity of chronic respiratory disease.	Feed for 5 to 8 d, do not use in birds producing eggs for food purposes; withdraw 48 h before slaughter.	
	Hygromycin B 8 to 12	Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; control of infestation of large round worms (<i>Heterakis gallinae</i>) and capillary worms (<i>Capillaria obsignata</i>).	Feed according to subtable in item (i).	
	Penicillin 2.4 to 50	1. Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; growth promotion and feed efficiency. 2. Turkeys; prevention of coccidiosis; growth promotion and feed efficiency.	As procaine penicillin. do.....	
	Penicillin plus streptomycin 90 to 180 (of combination).	1. Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; treatment of chronic respiratory disease (air-sac infection), blue comb (non-specific infectious enteritis). 2. Turkeys; prevention of coccidiosis; treatment of infectious sinusitis, blue comb (mud fever), hexamitiasis.	Feed contains 16.7% penicillin; as procaine penicillin; as streptomycin sulfate. Feed contains not less than 2.4 g of penicillin nor less than 12 g of streptomycin; as procaine penicillin; as streptomycin sulfate.	
	Roxarsone 22.7 to 45.4 (0.0025% to 0.005%).	1. Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; growth promotion and feed efficiency; improving pigmentation. 2. Turkeys; prevention of coccidiosis; growth promotion and feed efficiency; improving pigmentation.	Withdraw 5 d before slaughter; as sole source of organic arsenic. do.....	
(v) 227 (0.025%)		Laying chickens; treatment of coccidiosis.	For severe outbreaks of coccidiosis; administer for 2 weeks.	

¹ Bacitracin zinc in § 510.600(c) of this chapter.

(3) **Pheasants.** It is used as follows:

(i) **Amount.** 0.0175 percent (159 grams per ton).

(ii) **Indications for use.** For the prevention of coccidiosis in growing pheasants caused by *Eimeria colchici*, *E. duodenalis*, and *E. phasiani*.

(iii) **Limitations.** Feed continuously as sole ration. Use as sole source of amprolium. Fertility, hatchability, and other reproductive data are not available on amprolium in breeding pheas-

ants. Do not use in feeds containing bentonite.

[41 FR 10985, Mar. 15, 1976; 41 FR 14367, Apr. 5, 1976, as amended at 41 FR 16933, Apr. 23, 1976; 42 FR 18615, Apr. 8, 1977; 42 FR 36995, July 19, 1977; 43 FR 4006, Jan. 31, 1978; 43 FR 9804, Mar. 10, 1978; 43 FR 53717, Nov. 17, 1978; 46 FR 46797, Sept. 22, 1981; 47 FR 35188, Aug. 13, 1982; 47 FR 41106, Sept. 17, 1982; 50 FR 18472, May 1, 1985; 51 FR 7395, Mar. 3, 1986; 52 FR 2684, Jan. 26, 1987; 52 FR 6649, Mar. 4, 1987]

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21 CFR Ch. I (4-1-89 Ed)

§ 558.58 Amprolium and ethopabate.

(a) *Approvals.* Type A medicated articles: (1) 25 percent amprolium and 0.8 percent ethopabate; 25 percent amprolium and 8 percent ethopabate; 5 percent amprolium and 0.16 percent ethopabate; 5 percent amprolium and 1.6 percent ethopabate; to 000006.

(2) 0.15 percent amprolium and 0.004 percent ethopabate and 0.05 gram per

pound bacitracin (as bacitracin zinc salt) to 04701 § 510.600(c) of this chapter.

(b) *Special considerations.* Do not use in Type B or Type C medicated feeds containing bentonite.

(c) *Related tolerances.* See §§ 510.600 and 556.260 of this chapter.

(d) *Conditions of use.* (1) It is for chickens as follows:

Amprolium and ethopabate in grams per ton	Combination in grams per ton	Indications for use	Limitations	SP
(i) Amprolium 113.5 (0.0125 pct) and ethopabate 3.6 (0.0004 pct).		Broiler chickens as an aid in the prevention of coccidiosis.	Not for laying hens; as sole source of amprolium.	
(ii) Amprolium 113.5 (0.0125%) and ethopabate 3.6 (0.0004%).	Bambermycins 2 to 3 plus roxarsone 22.8 to 34.1 (0.0025% to 0.00375%).	Broiler chickens; as an aid in the prevention of coccidiosis; for increased rate of weight gain, improved feed efficiency, and pigmentation.	Feed continuously as the sole ration; as sole source of amprolium and organic arsenic; amprolium and ethopabate as provided by No. 000006 in § 510.600(c) of this chapter, roxarsone by No. 017210, bambermycins by No. 012799; withdraw 5 d before slaughter.	
	Lincomycin 2 to 4.....	Broiler chickens; for increase in rate of weight gain; improved feed efficiency; as an aid in the prevention of coccidiosis.	Not for laying chickens; as lincomycin hydrochloride monohydrate; as sole source of amprolium.	
	Lincomycin 2 to 4 plus roxarsone 45.4 (0.005%).	Broiler chickens; for increase in rate of weight gain; improved feed efficiency and pigmentation; as an aid in the prevention of coccidiosis.	Not for laying chickens; as lincomycin hydrochloride monohydrate; withdraw 5 d before slaughter; as sole source of amprolium and organic arsenic.	
	Roxarsone 45.4 (0.005 pct).	Broiler chickens; to aid in prevention of coccidiosis where severe exposure to coccidiosis from <i>Eimeria acervulina</i> , <i>E. maxima</i> , and <i>E. brunetti</i> is likely to occur; for increased rate of weight gain in broiler chickens raised in floor pens.	Do not feed to laying chickens; withdraw 5 d before slaughter; as sole source of amprolium; do not use as a treatment for outbreaks of coccidiosis; feed as sole ration from time chickens are placed on litter until the past the time when coccidiosis is ordinarily a hazard; roxarsone as provided by No. 017210 in § 510.600(c) of this chapter; combinations as provided by No. 000006.	
(iii) Amprolium 113.5 (0.0125%) and ethopabate 36.3 (0.004%).		Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; as an aid in the prevention of coccidiosis where severe exposure to coccidiosis from <i>Eimeria acervulina</i> , <i>E. maxima</i> , and <i>E. brunetti</i> is likely to occur.	Not for chickens over 16 weeks of age.	
	Arsenilic acid 90 (0.01 pct) plus erythromycin 4.6 to 18.5.	Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; growth promotion and feed efficiency; improve pigmentation.	Not for laying hens; withdraw 5 d before slaughter; as sole source of organic arsenic; as erythromycin thiocyanate.	

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Amprolium and ethopabate in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
(ii) Amprolium 113.5 (0.0125%) and ethopabate 36.3 (0.004%).	Bacitracin 4 to 50.....	1. Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; to aid in prevention of coccidiosis where severe exposure to coccidiosis from <i>Eimeria acervulina</i> , <i>E. maxima</i> , and <i>E. brunetti</i> is likely to occur; for increased rate of weight gain in broiler chickens raised in floor pens.	Not for chickens over 16 weeks of age; do not feed to laying chickens; as sole source of amprolium; not for use as a treatment for outbreaks of coccidiosis; as bacitracin methylene disalicylate as provided by No. 046573 or bacitracin zinc as provided by No. 011716 in § 510.600(c) of this chapter; feed as the sole ration from the time chickens are placed on litter until past the time when coccidiosis is ordinarily a hazard; combination as provided by No. 000006 in § 510.600(c) of this chapter.	011716
		2. Broiler chickens; as an aid in prevention of coccidiosis where severe exposure to coccidiosis from <i>Eimeria acervulina</i> , <i>E. maxima</i> , and <i>E. brunetti</i> is likely to occur; improved feed efficiency.	Not for chickens over 16 weeks of age; do not feed to laying chickens; as sole source of amprolium; not for use as a treatment for coccidiosis; bacitracin zinc as provided by No. 011716 in § 510.600(c) of this chapter; feed as the sole ration from the time chickens are placed on litter until market weight; combination as provided by No. 011716.	
	Bacitracin 5 to 35 plus roxarsone 34 (0.00375%).	Broiler chickens; for increased rate of weight gain and as an aid in the prevention of coccidiosis where severe exposure to coccidiosis from <i>Eimeria acervulina</i> , <i>E. maxima</i> , and <i>E. brunetti</i> is likely to occur in broiler chickens raised in floor pens.	Do not feed to laying chickens; withdraw 5 d before slaughter; as sole source of amprolium and organic arsenic; do not use as a treatment for outbreaks of coccidiosis; feed as the sole ration from time chickens are placed on litter until past the time when coccidiosis is ordinarily a hazard; amprolium and ethopabate as provided by No. 000006 in § 510.600(c) of this chapter; bacitracin methylene disalicylate as provided by No. 046573 or bacitracin zinc as provided by No. 011716 in § 510.600(c) of this chapter; roxarsone as provided by No. 017210 in § 510.600(c) of this chapter; combination as provided by No. 000006 in § 510.600(c) of this chapter.	

Amprolium and ethopabate in grams per ton	Combination in grams per ton	Indications for use	Limitations
(ii) Amprolium 113.5 (0.0125%) and ethopabate 36.3 (0.004%).	Bacitracin 20 to 35 plus roxarsone 34 (0.00375%).	Broiler chickens; for increased rate of weight gain, improved feed efficiency, and as an aid in the prevention of coccidiosis where severe exposure to coccidiosis from <i>Eimeria acervulina</i> , <i>E. maxima</i> , and <i>E. brunetti</i> is likely to occur in broiler chickens raised in floor pens.	Do not feed to laying chickens; withdraw 5 d before slaughter; as sole source of amprolium and organic arsenic; do not use as a treatment for outbreaks of coccidiosis; feed as the sole ration from time chickens are placed on litter until past the time when coccidiosis is ordinarily a hazard; amprolium and ethopabate as provided by No. 000006 in § 510.600(c) of this chapter; bacitracin methylene disalicylate as provided by No. 048573 in § 510.600(c) of this chapter; roxarsone as provided by No. 017210 in § 510.600(c) of this chapter; combination as provided by No. 000008 in § 510.600(c) of this chapter.
	Bacitracin 10 to 50 plus roxarsone 15.4 to 45.4 (0.0017% to 0.005%).	Broiler chickens; as an aid in prevention of coccidiosis where severe exposure to coccidiosis from <i>Eimeria acervulina</i> , <i>E. maxima</i> , and <i>E. brunetti</i> is likely to occur; improved feed efficiency.	Do not feed to laying chickens; withdraw 5 d before slaughter; as sole source of amprolium and organic arsenic; do not use as a treatment for outbreaks of coccidiosis; feed as the sole ration from time chicks are placed on litter until past the time when coccidiosis is ordinarily a hazard; amprolium and ethopabate as provided by No. 000006 in § 510.600(c) of this chapter; bacitracin zinc as provided by No. 011716; roxarsone as provided by No. 017210; combination as provided by No. 011716.
	Bacitracin 10 plus roxarsone 30 to 45.4 (0.0033% to 0.005%).	Broiler chickens; as an aid in prevention of coccidiosis where severe exposure to coccidiosis from <i>E. acervulina</i> , <i>E. maxima</i> , and <i>E. brunetti</i> is likely to occur; improved feed efficiency and improved pigmentation.	do
	Bambermycins 1 to 3...	Broiler chickens; as an aid in the prevention of coccidiosis where severe exposure to coccidiosis from <i>Eimeria acervulina</i> , <i>E. maxima</i> , and <i>E. brunetti</i> is likely to occur; for increased rate of weight gain, and improved feed efficiency.	Feed continuously as the sole ration; as sole source of amprolium; amprolium, ethopabate as provided by No. 000006 in § 510.600(c) of this chapter, bambermycins as provided by No. 012799 in § 510.600(c) of this chapter.
	Bambermycins 1 to 3 plus roxarsone 22.8 to 34.1 (0.0025% to 0.00375%).	Broiler chickens; as an aid in the prevention of coccidiosis where severe exposure to coccidiosis from <i>Eimeria acervulina</i> , <i>E. maxima</i> , and <i>E. brunetti</i> is likely to occur; for increased rate of weight gain; improved feed efficiency, and improved pigmentation.	Feed continuously as the sole ration; as sole source of amprolium and organic arsenic; amprolium and ethopabate as provided by No. 000006 in § 510.600(c) of this chapter, roxarsone by No. 017210, bambermycins by No. 012799. Withdraw 5 days before slaughter.

Amprolium and ethopabate in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
(v) Amprolium 113.5 to 227 (0.0125% to 0.025%) and ethopabate 3.6 (0.0004%).	Erythromycin 4.6 to 18.5.	Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; growth promotion and feed efficiency.	Not for laying hens; withdraw 24 hours before slaughter; erythromycin thiocyanate.	00007
	Virginiamycin, 15	Broiler chickens, as an aid in the prevention of coccidiosis where severe exposure to <i>Eimeria acervulina</i> , <i>E. brunetti</i> , and <i>E. maxima</i> is likely to occur, for increased rate of weight gain and improved feed efficiency.	Feed continuously as sole ration, do not feed to laying hens, not for chickens over 16 weeks of age, as sole source of amprolium, amprolium and ethopabate as provided by 000006 in § 510.600(c), virginiamycin as provided by 000007.	
	Virginiamycin, 5 to 15	Broiler chickens, as an aid in the prevention of coccidiosis where severe exposure to <i>Eimeria acervulina</i> , <i>E. brunetti</i> , and <i>E. maxima</i> is likely to occur, for increased rate of weight gain.	do	
		For broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis.	Not for laying hens	
	Arsenic acid 90 (0.01%).	Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; growth promotion and feed efficiency; improving pigmentation.	As sole source of organic arsenic; withdraw 5 d before slaughter; not for laying hens.	
	Arsenic acid 90 (0.01%) plus erythromycin 92.5.	1. For broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; as an aid in the prevention of chronic respiratory disease during periods of stress; growth promotion and feed efficiency; improving pigmentation. 2. For broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; as an aid in the prevention of infectious coryza; growth promotion and feed efficiency; improving pigmentation.	Feed for 2 d before stress and 3 to 6 d after stress; withdraw 5 d before slaughter; as sole source of organic arsenic; not for laying hens. Feed for 7 to 14 d; withdraw 5 d before slaughter; as sole source of organic arsenic; not for laying hens.	
	Arsenic acid 90 (0.01%) plus erythromycin 165.	For broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; as an aid in the prevention and reduction of lesions and in lowering severity of chronic respiratory disease; growth promotion and feed efficiency; improving pigmentation.	Feed for 5 to 8 d; do not use in birds producing eggs for food purposes; withdraw 5 d before slaughter; as sole source of organic arsenic.	
	Bacitracin 4 to 50	For broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; growth promotion and feed efficiency.	As bacitracin methylene disilicate, not for laying hens.	

Amprolium and ethopabate in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sp
	Bacitracin 100 to 200	1. Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; treatment of chronic respiratory disease (air-sac infection) and blue comb (nonspecific infectious enteritis). 2. For broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; treatment of chronic respiratory disease (air-sac infection), blue comb (nonspecific infectious enteritis).	do As zinc bacitracin, not for laying hens.	
	Bacitracin 4 to 50 plus roxarsone 22.7 to 45.4 (0.0025% to 0.005%).	Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; growth promotion and feed efficiency; improving pigmentation.	As bacitracin methylene disacrylate; not for laying hens; as sole source of organic arsenic; withdraw 5 d before slaughter.	
	Chlortetracycline 100 to 200	For broiler chickens and for replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; treatment of chronic respiratory disease (air-sac infection), blue comb (nonspecific infectious enteritis); prevention of synovitis.	Not for laying hens; as chlortetracycline hydrochloride.	
	Chlortetracycline 200	Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; treatment of chronic respiratory disease caused by strains of <i>Mycoplasma gallisepticum</i> susceptible to chlortetracycline.	In low calcium feed containing 0.8% dietary calcium and 1.5% sodium sulfate; feed continuously as sole ration for not more than the 1st 3 weeks of life; not for laying hens.	
	Erythromycin 92.5	1. For broiler chickens and for replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; as an aid in the prevention of chronic respiratory disease during periods of stress. 2. For broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; as an aid in the prevention of infectious coryza.	Feed for 2 d before stress and 3 to 6 d after stress; withdraw 24 h before slaughter; not for laying hens. Feed for 7 to 14 d; withdraw 24 h before slaughter; not for laying hens.	
	Erythromycin 185	For broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; as an aid in the prevention and reduction of lesions and in lowering severity of chronic respiratory disease.	Feed for 5 to 6 d; do not use in birds producing eggs for food purposes; withdraw 48 h before slaughter.	

Amprolium and ethopabate in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
	Penicillin 2.4 to 50	For broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; growth promotion and feed efficiency; improving pigmentation.	Not for laying hens; as procaine penicillin.	
	Penicillin plus streptomycin 90 to 180 (of combination).	For broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; treatment of chronic respiratory disease (air-sac infection), blue comb (non-specific infectious enteritis).	Feed contains 16.7% penicillin; as procaine penicillin; as streptomycin sulfate; not for laying hens.	
	Roxarsone 22.7 to 45.4 (0.0025% to 0.005%).	Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis; growth promotion and feed efficiency; improving pigmentation.	As sole source of organic arsenic; withdraw 5 d before slaughter; not for laying hens.	
(4) Amprolium 136.2 (0.015%) and ethopabate 3.6 (0.0004%).	Bacitracin 10	Broiler chickens; as an aid in the prevention of coccidiosis; growth promotion and feed efficiency.	Feed as sole ration; use as sole source of amprolium; do not feed to laying hens; as bacitracin methylene disalicylate.	047019

[41 FR 10990, Mar. 15, 1976; 41 FR 14367, Apr. 5, 1976; 41 FR 16550, Apr. 20, 1976]

EDITORIAL NOTE: For FEDERAL REGISTER citations affecting § 558.58, see the List of CFR Sections Affected in the Finding Aid section of this volume.

§ 558.59 Apramycin.

(a) *Approvals.* Type A articles to sponsors identified in § 510.600(c) of this chapter as follows:

(1) 000986 for 75 grams apramycin (as apramycin sulfate) per pound for use as in paragraph (d)(1) of this section.

(2) [Reserved]

(b) [Reserved]

(c) *Related tolerances.* See § 556.52 of this chapter.

(d) *Conditions of use—(1) Swine—(i) Amount.* 150 grams per ton.

(ii) *Indications for use.* For control of porcine colibacillosis (weanling pig scours) caused by susceptible strains of *Escherichia coli*.

(iii) *Limitations.* Use for 14 days. Withdraw 28 days before slaughter.

(2) [Reserved]

[51 FR 9190, Mar. 18, 1986]

§ 558.60 Arsanilate sodium.

(a) *Approvals.* Type A medicated articles: 20, 50, or 100 percent to 015565 in § 510.600(c) of this chapter.

(b) *Related tolerances.* See § 556.60 of this chapter.

(c) *Conditions of use.* (1) It is used for chickens and turkeys as follows:

(i) *Grams per ton.* 90 (0.01 percent).

(ii) *Indications for use.* For growth promotion and feed efficiency; improving pigmentation.

(iii) *Limitations.* Withdraw 5 days before slaughter; as sole source of organic arsenic.

(2) Arsanilate sodium may be used in accordance with the provisions of this section in the combinations provided as follows:

(i) Amprolium in accordance with § 558.55.

(ii) Zoalene in accordance with § 558.680.

[41 FR 10992, Mar. 15, 1976, as amended at 51 FR 7395, Mar. 3, 1986; 51 FR 33897, Sept. 24, 1986]

§ 558.62 Arsanilic acid.

(a) *Approvals.* Type A medicated articles: 20, 50, or 100 percent to 015565 in § 510.600(c) of this chapter.

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(b) *Related tolerances.* See § 558.60 of this chapter.

(c) *Conditions of use.* (1) It is for chickens and turkeys as follows:

Arsanilic acid in grams per ton	Combination in grams per ton	Indications for use	Limitations
90 (0.01%)		1. Chickens; growth promotion and feed efficiency; improving pigmentation. 2. Turkeys; growth promotion and feed efficiency; improving pigmentation.	Withdraw 5 d before slaughter; as sole source of organic arsenic.
	Erythromycin 4.6 to 18.5	Chickens; growth promotion and feed efficiency; improving pigmentation.	As erythromycin thiocyanate; withdraw 5 d before slaughter; as sole source of organic arsenic.
	Erythromycin 92.5	1. Chickens; as an aid in the prevention of chronic respiratory disease during periods of stress; growth promotion and feed efficiency; improving pigmentation. 2. Chickens; as an aid in the prevention of infectious coryza; growth promotion and feed efficiency; improving pigmentation.	As erythromycin thiocyanate; feed for 2 d before stress and 3 to 6 d after stress; withdraw 5 d before slaughter; as sole source of organic arsenic.
	Erythromycin 185	Chickens; as an aid in the prevention and reduction of lesions and in lowering severity of chronic respiratory disease; growth promotion and feed efficiency; improving pigmentation.	As erythromycin thiocyanate; feed for 7 to 14 d; withdraw 5 days before slaughter; as sole source of organic arsenic.

(2) Arsanilic acid may be used in accordance with the provisions of this section in the combinations provided as follows:

- (i) Amprolium in accordance with § 558.55.
- (ii) Amprolium and ethopabate in accordance with § 558.58.
- (iii) Bacitracin zinc in accordance with § 588.78.
- (iv) Bacitracin and zoalene in accordance with § 558.680.
- (v) Buquinolate in accordance with § 558.105.
- (vi) Zolene in accordance with § 558.680.

[41 FR 10992, Mar. 15, 1976, as amended; 42 FR 18617, Apr. 8, 1977; 51 FR 7395, M. 3, 1986; 51 FR 33897, Sept. 24, 1986]

§ 558.76 Bacitracin methylene disalicylate

(a) *Approvals.* Type A medicated articles: 10, 25, 30, 40, 50, 60, or 75 grams per pound to 046573 in § 510.600(c) of this chapter.

(b) *Special considerations.* The quantities of antibiotics are expressed in terms of the equivalent amount antibiotic standard.

(c) *Related tolerances.* See § 558.60 of this chapter.

(d) *Conditions of use.* (1) It is used as follows:

Bacitracin methylene disalicylate in grams per ton	Combination in grams per ton	Indications for use	Limitations
(i) 4 to 50		Chickens, turkeys, and pheasants; increased rate of weight gain and improved feed efficiency ¹ .	
(ii) 5 to 20		Quail not over 5 weeks of age; increased rate of weight gain and improved feed efficiency ¹ .	

Bacitracin methylene disalicylate in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
(a) 10 to 25		Chickens; for increased egg production and improved feed efficiency for egg production.	For first 7 months of production.	046573
(a) 10 to 30		Swine; for increased rate of weight gain and improved feed efficiency.	For growing and finishing swine.	046573
(v) [Reserved]				
(a) 50		Broiler chickens; as an aid in the prevention of necrotic enteritis caused or complicated by <i>Clostridium</i> spp. or other organisms susceptible to bacitracin.		046573
(vi)-(vii) [Reserved]				
(a) 100 to 200		Broiler chickens; as an aid in the control of necrotic enteritis caused or complicated by <i>Clostridium</i> spp. or other organisms susceptible to bacitracin.		046573
(a) 200		Turkeys; as an aid in the control of transmissible enteritis in growing turkeys complicated by organisms susceptible to bacitracin methylene disalicylate.		046573
		Quail; for the prevention of ulcerative enteritis in growing quail due to <i>Clostridium colinum</i> susceptible to bacitracin methylene disalicylate.	From Type A medicated articles containing 25, 40, or 50 grams of bacitracin methylene disalicylate. Feed continuously as the sole ration.	046573
(a) 250		Swine: For control of swine dysentery associated with <i>Treponema hyodysenteriae</i> on premises with a history of swine dysentery but where signs of the disease have not yet occurred; or following an approved treatment of the disease condition.	As the sole ration. Not for use in swine weighing more than 250 pounds. Diagnosis should be confirmed by a veterinarian when results are not satisfactory.	046573

¹ These conditions are NAS/NRC reviewed and found effective. Applications for these uses may not require effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(2) It is used as bacitracin methylene disalicylate in feed for animals as follows:

(i) Amount. 70 milligrams per head per day.

(a) Indications for use. Feedlot beef cattle; reduction in the number of liver condemnations due to abscesses.

(b) Limitations. Administer continuously throughout the feeding period.

(ii) Amount. 250 milligrams per head per day.

(a) Indications for use. Feedlot beef cattle; reduction in the number of liver condemnations due to abscesses.

(b) Limitations. Administer continuously for 5 days then discontinue for subsequent 25 days, repeat the pattern during the feeding period.

(3) It is used as bacitracin methylene disalicylate in accordance with the provisions of this section in the combinations provided as follows:

(i) Amprolium in accordance with § 558.55.

(ii) Amprolium with ethopabate in accordance with § 558.58.

(iii) Arsanilic acid with zoalene in accordance with § 558.680.

(iv) Carbarsone (not U.S.P.) in accordance with § 558.120.

(v) [Reserved]

(vi) Hygromycin B in accordance with § 588.274.

(vii) Monensin in accordance with § 588.355.

(viii) Lasalocid sodium alone or with roxarsone as in § 558.311.

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(ix) Monensin and roxarsone in accordance with § 558.355.

(x) Salinomycin alone or with roxarsone as in § 558.550.

(xi) Halofuginone hydrobromide and roxarsone in accordance with § 558.265.

(xii) Halofuginone in accordance with § 558.265.

[41 FR 10993, Mar. 15, 1976]

EDITORIAL NOTE: For FEDERAL REGISTER citations affecting § 558.78, see the List of CFR Sections Affected in the Finding Aids section of this volume.

§ 558.78 Bacitracin zinc.

(a) *Approvals.* Type A medicated articles: (1) 50 grams per pound to

046573 in § 510.600(c) of this chapter for use as in paragraph (d)(1) of this section.

(2) 10, 25, 40, and 50 grams per pound to 011716 in § 510.600(c) of this chapter for use as in paragraph (d)(1)(i) of this section.

(3) 5 and 50 grams per pound to 000010 in § 510.600(c) of this chapter for use in chickens as in paragraph (d)(1)(i) of this section.

(b) *Special considerations.* Quantities of antibiotics are expressed in terms of the equivalent amount of antibiotic standard.

(c) *Related tolerances.* See § 558.78 of this chapter.

(d) *Conditions of use.* (1) It is as follows:

Bacitracin zinc in grams per ton	Combinations in grams per ton	Indications for use	Limitations
(i) 4 to 50		Chickens, turkeys, and pheasants; for increased rate of weight gain and improved feed efficiency ¹ .	Growing chickens, turkeys, and pheasants ¹ .
(ii) 5 to 20		Quail; for increased rate of weight gain and improved feed efficiency ¹ .	Growing quail; feed as the Type C feed to starting quail through 5 weeks of age ¹ .
(iii) 10 to 25		Laying chickens; improved feed efficiency and increased egg production.	
(iv) 10 to 50		Swine; increased rate of weight gain and improved feed efficiency.	Growing and finishing swine
(v) 20		Growing-finishing swine; increased rate of weight gain.	In Type C feed.
(vi) 20 to 40		Growing-finishing swine; improved feed efficiency.	do

¹ These conditions are NAS/NRC reviewed and found effective. Applications for their uses may not require effect data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(2) It is used in feed for growing cattle at 35 to 70 milligrams per head per day as follows:

(i) To aid in stimulating growth and improving feed efficiency.

(ii) For increased rate of weight gain and improved feed efficiency; see sponsor 011716.

(3) Bacitracin zinc is used in accordance with the provisions of this section in combination with:

(i) Amprolium as in § 558.55.

(ii) Amprolium with ethopabate as in § 558.58.

(iii) Arsanilic acid and zoalene as in § 558.680.

(iv) [Reserved]

(v) Hygromycin B as in § 558.274.

(vi) Monensin as in § 558.355.

(vii) Zoalene as in § 558.680.

(viii) Lasalocid sodium and roxarsone as in § 558.311.

(ix) Monensin and roxarsone as in § 558.355.

(x) Salinomycin alone or with roxarsone as in § 558.550.

(xi) Carbarsone as in § 558.120.

[41 FR 10994, Mar. 15, 1976]

EDITORIAL NOTE: For FEDERAL REGISTER citations affecting § 558.78, see the List of CFR Sections Affected in the Finding Aids section of this volume.

§ 558.95 Bambermycins.

(a) *Approvals.* Type A medicated articles: (1) 2 and 10 grams of active ingredient per pound to 012799 in § 510.600(c) of this chapter for use as in paragraph

(b)(1), (2)(i) and (ii), and (3) of this section.

(2) 0.4 gram of activity per pound to 012799 and 020275 for use as in paragraph (b)(2) of this section.

(3) 0.4 and 2 grams of activity per pound to 011490 in § 510.600(c) of this chapter for use as in paragraph (b)(2) of this section.

(4) 0.4 and 2 grams of activity per pound for use as in paragraph (b)(2) of this section and 2 grams of activity per pound for use as in paragraph (b)(3) of this section to 016968, 017274, and 017790 in § 510.600(c) of this chapter.

(5) 0.08 gram of activity per pound for use as in paragraph (b)(2) of this section to 034139 in § 510.600(c) of this chapter.

(b) *Conditions of use*—(1) *Broiler chicken*. It is used as follows:

(i) *Amount per ton*. 1 to 2 grams.

(a) *Indications for use*. For increased rate of weight gain and improved feed efficiency.

(b) *Limitations*. Feed continuously as the sole ration.

(ii) *Amount per ton*. Bambermycins, 1 to 3 grams plus amprolium, 113.5 grams (.0125 percent) plus ethopabate, 36.3 grams (.004 percent).

(a) *Indications for use*. As an aid in the prevention of coccidiosis where severe exposure to coccidiosis from *E. acervulina*, *E. maxima*, and *E. brunetti* is likely to occur. For increased rate of weight gain and improved feed efficiency.

(b) *Limitations*. Feed continuously as the sole ration; as sole source of amprolium; amprolium and ethopabate as provided by No. 000006 in § 510.600(c) of this chapter.

(iii) *Amount per ton*. Bambermycins, 1 to 3 grams plus amprolium, 113.5 grams (.0125 percent) plus ethopabate, 36.3 grams (.004 percent) plus roxarsone, 22.8 to 34.1 grams (.0025-.00375 percent).

(a) *Indications for use*. As an aid in the prevention of coccidiosis where severe exposure to coccidiosis from *E. acervulina*, *E. maxima*, and *E. brunetti* is likely to occur. For increased rate of weight gain, improved feed efficiency, and improved pigmentation.

(b) *Limitations*. Feed continuously as the sole ration; as sole source of amprolium and organic arsenic; ampro-

lium and ethopabate as provided by No. 000006 in § 510.600(c) of this chapter, roxarsone as provided by No. 017210 in § 510.600(c) of this chapter. Withdraw 5 days before slaughter.

(iv) *Amount per ton*. Bambermycins, 1 to 3 grams plus amprolium, 113.5 grams (.0125 percent) plus ethopabate, 36.3 grams (.004 percent) plus roxarsone, 22.8 to 34.1 grams (.0025-.00375 percent).

(a) *Indications for use*. As an aid in the prevention of coccidiosis. For increased rate of weight gain, improved feed efficiency, and improved pigmentation.

(b) *Limitations*. Feed continuously as the sole ration; as sole source of amprolium and organic arsenic; amprolium and ethopabate as provided by No. 000006 in § 510.600(c) of this chapter, roxarsone as provided by No. 017210 in § 510.600(c) of this chapter. Withdraw 5 days before slaughter.

(v) *Amount per ton*. Bambermycins, 1 to 3 grams plus amprolium, 113.5 grams (.0125 percent) plus roxarsone, 22.8 to 34.1 grams (.0025-.00375 percent).

(a) *Indications for use*. As an aid in the prevention of coccidiosis. For increased rate of weight gain, improved feed efficiency, and improved pigmentation.

(b) *Limitations*. Feed continuously as the sole ration; as sole source of amprolium and organic arsenic; amprolium as provided by No. 000006 in § 510.600(c) of this chapter, roxarsone as provided by No. 017210 in § 510.600(c) of this chapter. Withdraw 5 days before slaughter.

(vi) *Amount per ton*. Bambermycins, 1 to 2 grams plus monensin, 90 to 110 grams.

(a) *Indications for use*. For increased rate of weight gain and improved feed efficiency; as an aid in the prevention of coccidiosis caused by *E. necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mitis*, and *E. maxima*.

(b) *Limitations*. Do not feed to laying chickens; feed continuously as sole ration; as monensin sodium provided by No. 000986 in § 510.600(c) of this chapter; as bambermycins provided by No. 012799 in § 510.600(c) of this chapter.

(vii) *Amount per ton.* Bambermycins, 1 gram plus monensin, 90 to 110 grams plus roxarsone, 22.7 to 45.4 grams (0.0025 to 0.005 percent).

(a) *Indications for use.* For increased rate of weight gain and improved feed efficiency; as an aid in the prevention of coccidiosis caused by *E. necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*.

(b) *Limitations.* Do not feed to laying chickens; feed continuously as sole ration; use as sole source of organic arsenic; withdraw 5 days before slaughter; as monensin sodium provided by No. 000986 in § 510.600(c) of this chapter; as bambermycins provided by No. 012799 in § 510.600(c) of this chapter; as roxarsone provided by No. 017210 in § 510.600(c) of this chapter.

(viii) *Amount per ton.* Bambermycins, 1 gram plus zoalene, 113.4 grams (0.0125 percent).

(a) *Indications for use.* As an aid in the prevention and control of coccidiosis; for increased rate of weight gain and improved feed efficiency.

(b) *Limitations.* Do not feed to chickens over 14 weeks of age; feed continuously as sole ration; zoalene as provided by No. 025700, roxarsone as provided by No. 017210 in § 510.600(c) of this chapter.

(ix) *Amount per ton.* Bambermycins, 1 gram plus zoalene, 113.4 grams (0.0125 percent) plus roxarsone, 22.7 grams (0.0025 percent).

(a) *Indications for use.* As an aid in the prevention and control of coccidiosis; for increased rate of weight gain and improved feed efficiency.

(b) *Limitations.* Do not feed to chickens over 14 weeks of age; feed continuously as sole ration; feed as sole source of organic arsenic; withdraw 5 days before slaughter; zoalene as provided by No. 025700, roxarsone as provided by No. 017210 in § 510.600(c) of this chapter.

(x) *Amount per ton.* Bambermycins, 1 gram plus lasalocid sodium, 68 to 113 grams (0.0075 to 0.0125 percent) plus roxarsone, 45.4 grams (0.005 percent).

(a) *Indications for use.* For prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*; as an aid in the reduction of lesions due to *E. tenella*; and for increased rate of weight gain.

(b) *Limitations.* For broiler chicks only; feed continuously as sole ration; withdraw 5 days before slaughter; roxarsone as provided by Nos. 017210, 011801 in § 510.600(c) of this chapter and lasalocid sodium as provided by No. 000004 in § 510.600(c) of this chapter.

(xi) *Amount per ton.* Bambermycins, 1 to 2 grams, plus roxarsone, 22.7 to 45.4 grams, and salinomycin 40 to 60 grams.

(a) *Indications for use.* For prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*, including some field strains of *E. tenella* that are more susceptible to roxarsone combined with salinomycin than roxarsone alone; and for improved feed efficiency.

(b) *Limitations.* For broiler chicks only; do not feed to laying chickens; feed continuously as sole ration; use as sole source of organic arsenic; withdraw 5 days before slaughter; not approved for use with pellet binder; may be fatal if accidentally fed to adult turkeys or horses; as roxarsone provided by No. 011801 or 017210 in § 510.600(c) of this chapter; as salinomycin sodium biomass provided by No. 000031 in § 510.600(c) of this chapter.

(xii) *Amount per ton.* Bambermycins, 1 to 3 grams, plus salinomycin 40 to 60 grams.

(a) *Indications for use.* For prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*; and improved feed efficiency.

(b) *Limitations.* For broiler chicks only; Do not feed to laying chickens; feed continuously as sole ration; not approved for use with pellet binder; may be fatal if accidentally fed to adult turkeys or horses; as salinomycin sodium biomass provided by No. 000031 in § 510.600(c) of this chapter.

(xiii) *Amount per ton.* Bambermycins, 1 to 2 grams plus monensin, 90 to 110 grams plus roxarsone, 22.7 to 45.4 grams (0.0025 to 0.005 percent).

(a) *Indications for use.* For increased rate of weight gain; as an aid in prevention of coccidiosis caused by *E. necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*.

(b) *Limitations.* See paragraph (e)(1)(vii)(b) of this section.

(2) *Growing-finished swine.* It is used as follows:

(i) *Amount per ton.* 2 grams.

(a) *Indications for use.* For increased rate of weight gain and improved feed efficiency.

(b) *Limitations.* Feed continuously as sole ration.

(ii) *Amount per ton.* 2 to 4 grams.

(a) *Indications for use.* For increased rate of weight gain.

(b) *Limitations.* Feed continuously as sole ration.

(3) *Growing turkeys.* It is used as follows:

(i) *Amount per ton.* 1 to 2 grams.

(a) *Indications for use.* For improved feed efficiency.

(b) *Limitations.* Feed continuously as the sole ration.

(ii) *Amount per ton.* 2 grams.

(a) *Indications for use.* For increased rate of weight gain and improved feed efficiency.

(b) *Limitations.* Feed continuously as sole ration.

(iii) *Amount per ton.* Bambermycins, 1 to 4 grams plus amprolium, 113.5 grams (.0125 percent).

(a) *Indications for use.* For prevention of coccidiosis; for increased rate of weight gain and improved feed efficiency.

(b) *Limitations.* Feed continuously as the sole source of amprolium; amprolium as provided by No. 000006 in § 510.600(c) of this chapter.

(iv) *Amount per ton.* Bambermycins, 1 or 4 grams plus carbarsone, 227 grams (0.025 percent).

(a) *Indications for use.* For improved feed efficiency (1 gram per ton) or increased rate of weight gain (4 grams per ton); as an aid in the prevention of blackhead.

(b) *Limitations.* Feed continuously 2 weeks before blackhead is expected and continue as long as prevention is needed; withdraw 5 days before slaughter; use as sole source of organic arsenic; carbarsone by 011794 in § 510.600(c) of this chapter.

(4) Bambermycins may be used as in this section in combination with:

(i) Halofuginone as in § 558.265.

(ii) Narasin as in § 558.363.

[40 FR 13959, Mar. 27, 1975]

EDITORIAL NOTE: For FEDERAL REGISTER citations affecting § 558.95, see the List of

CFR Sections Affected in the Finding Aids section of this volume.

§ 558.105 Buquinolate.

(a) *Approvals.* Type A medicated articles: 16.5 and 22 percent to 000149 in § 510.600(c) of this chapter.

(b) *Special considerations.* Do not use in Type B or Type C medicated feeds containing bentonite.

(c) *Related tolerances.* See § 556.90 of this chapter.

(d) *Conditions of use.* It is used as follows:

(1) *Broiler or fryer chickens—*(i) *Amount per ton.* Buquinolate, 75 grams (0.00825 percent).

(a) *Indications for use.* An aid in the prevention of coccidiosis caused by *E. tenella*, *E. maxima*, *E. necatrix*, *E. brunetti*, and *E. acervulina*.

(b) *Limitations.* Feed continuously as the sole ration.

(ii) *Amount per ton.* Buquinolate, 75 grams (0.00825 percent) plus arsanilic acid, 90 grams (0.01 percent).

(a) *Indications for use.* An aid in the prevention of coccidiosis caused by *E. tenella*, *E. maxima*, *E. necatrix*, *E. brunetti*, and *E. acervulina*; growth promotion and feed efficiency; improving pigmentation.

(b) *Limitations.* Feed continuously as the sole ration; withdraw 5 days before slaughter; as sole source of organic arsenic.

(iii) *Amount per ton.* Buquinolate, 75 grams (0.00825 percent) plus roxarsone, 22.7-45.4 grams (0.0025-0.005 percent).

(a) *Indications for use.* An aid in the prevention of coccidiosis caused by *E. tenella*, *E. maxima*, *E. necatrix*, *E. brunetti*, and *E. acervulina*; growth promotion and feed efficiency; improving pigmentation.

(b) *Limitations.* Feed continuously as the sole ration; withdraw 5 days before slaughter; as sole source of organic arsenic.

(iv) *Amount per ton.* Buquinolate, 75 grams (0.00825 percent) plus penicillin, 2.4-50 grams.

(a) *Indications for use.* An aid in the prevention of coccidiosis caused by *E. tenella*, *E. maxima*, *E. necatrix*, *E. brunetti*, and *E. acervulina*; growth promotion and feed efficiency.

(b) *Limitations.* Feed continuously as the sole ration; as procaine penicillin.

(v) *Amount per ton.* Buquinolate, 75 grams (0.00825 percent) plus bacitracin, 4-50 grams.

(a) *Indications for use.* An aid in the prevention of coccidiosis caused by *E. tenella*, *E. maxima*, *E. necatrix*, *E. brunetti*, and *E. acervulina*; growth promotion and feed efficiency.

(b) *Limitations.* Feed continuously as the sole ration; as zinc bacitracin or bacitracin methylene disalicylate.

(vi) *Amount per ton.* Buquinolate, 75 grams (0.00825 percent) plus penicillin + bacitracin, 3.6-50 grams.

(a) *Indications for use.* An aid in the prevention of coccidiosis caused by *E. tenella*, *E. maxima*, *E. necatrix*, *E. brunetti*, and *E. acervulina*; growth promotion and feed efficiency.

(b) *Limitations.* Feed continuously as the sole ration; not less than 0.6 gram of penicillin nor less than 3 grams of bacitracin; as procaine penicillin plus zinc bacitracin or bacitracin methylene disalicylate.

(vii) *Amount per ton.* Buquinolate, 75 grams (0.00825 percent) plus chlorotetracycline, 200 grams.

(a) *Indications for use.* An aid in the prevention of coccidiosis caused by *E. tenella*, *E. maxima*, *E. necatrix*, *E. brunetti*, and *E. acervulina*; treatment of chronic respiratory disease (air-sac infection), blue comb (nonspecific enteritis) prevention of synovitis.

(b) *Limitations.* In low calcium feed containing 0.8 percent dietary calcium and 1 percent to 1.5 percent sodium sulfate; to be fed continuously for not more than the first 21 days of life.

(viii) *Amount per ton.* Buquinolate, 75 grams (0.00825 percent) plus lincomycin, 2-4 grams.

(a) *Indications for use.* For increase in rate of weight gain and improved feed efficiency; as an aid in the prevention of coccidiosis caused *E. tenella*, *E. maxima*, *E. necatrix*, *E. brunetti*, *E. acervulina*.

(b) *Limitations.* For broiler and fryer chickens; feed continuously as the sole ration.

(ix) *Amount per ton.* Buquinolate, 75-100 grams (0.00825-0.011 percent) plus roxarsone, 22.7-34.0 grams (0.0025-0.00375 percent).

(a) *Indications for use.* An aid in the prevention of coccidiosis caused by *E. tenella*, *E. maxima*, *E. necatrix*, *E. brunetti*, and *E. acervulina*; growth promotion and feed efficiency; improvement of pigmentation.

(b) *Limitations.* Feed continuously as the sole ration; withdrawn before slaughter; as sole source of organic arsenic; as roxarsone; by sponsor No. 017210, see § 558.105 of this chapter.

(x) *Amount per ton.* Buquinolate, 100 grams (0.011 percent) plus bacitracin, 4-15 grams.

(a) *Indications for use.* An aid in the prevention of coccidiosis caused by *E. tenella*, *E. maxima*, *E. necatrix*, *E. brunetti*, and *E. acervulina*; growth promotion and rate of weight gain.

(b) *Limitations.* Feed continuously as the sole ration; as bacitracin methylene disalicylate provided by sponsor No. 046573, in § 510.600(c) of this chapter.

(xi) *Amount per ton.* Buquinolate, 100 grams (0.011 percent) plus bacitracin, 19-35 grams.

(a) *Indications for use.* An aid in the prevention of coccidiosis caused by *E. tenella*, *E. maxima*, *E. necatrix*, *E. brunetti*, and *E. acervulina*; growth promotion and rate of weight gain and improved feed efficiency.

(b) *Limitations.* For broiler or fryer chickens; feed continuously as the sole ration; as bacitracin provided by sponsor No. 046573, in § 510.600(c) of this chapter.

(2) *Broiler, fryer, roaster or meat chickens—(i) Amount per ton.* 75-100 grams (0.00825-0.011 percent).

(ii) *Indications for use.* An aid in the prevention of coccidiosis caused by *E. tenella*, *E. maxima*, *E. necatrix*, *E. brunetti*, and *E. acervulina*.

(iii) *Limitations.* Feed continuously as the sole ration; do not exceed 75 grams per ton (0.00825 percent) to replacement chickens at 2 weeks of age.

(3) *Laying or breeding chickens—(i) Amount per ton.* 75 grams (0.00825 percent).

(ii) *Indications for use.* An aid in the prevention of coccidiosis caused by *E. tenella*, *E. maxima*, *E. necatrix*, *E. brunetti*, and *E. acervulina*.

(iii) **Limitations.** Feed to caged layers for 2 weeks following caging; feed continuously to layers and breeders kept on floors while in production or until marketed.

[40 FR 13959, Mar. 27, 1975, as amended at 41 FR 1062, Jan. 6, 1976; 41 FR 53002, Dec. 2, 1976; 44 FR 67114, Nov. 23, 1979; 51 FR 7396, Mar. 3, 1986; 53 FR 20843, June 7, 1988]

§ 558.115 Carbadox.

(a) **Approvals.** Type A medicated articles: 2.2 percent (10 grams per pound) to 000069 in § 510.600(c) of this chapter.

(b) **Related tolerances.** See § 556.100 of this chapter.

(c) **Special considerations.** Do not use in Type B or Type C medicated feeds containing bentonite.

(d) **Conditions of use.** It is used for swine as follows:

(1) **Amount per ton.** 10-25 grams (0.0011-0.00275 percent).

(i) **Indications for use.** For increase in rate of weight gain and improvement of feed efficiency.

(ii) **Limitations.** Do not feed to swine weighing more than 75 pounds body weight; do not feed to swine within 10 weeks of slaughter; do not use in complete feeds containing less than 15 percent crude protein.

(3) **Amount per ton.** 50 grams (0.0055 percent).

(i) **Indications for use.** For control of swine dysentery (vibronic dysentery, bloody scours, or hemorrhagic dysentery); control of bacterial swine enteritis (salmonellosis or necrotic enteritis caused by *Salmonella choleraesuis*); increased rate of weight gain and improved feed efficiency.

(ii) **Limitations.** Do not feed to swine weighing more than 75 pounds body weight; do not feed to swine within 10 weeks of slaughter; do not use in complete feeds containing less than 15 percent crude protein.

(3) **Amount per ton.** Carbadox 50 grams (0.0055 percent) plus pyrantel tartrate, 96 grams (0.0106 percent).

(i) **Indications for use.** For control of swine dysentery (vibronic dysentery, bloody scours, or hemorrhagic dysentery); control of bacterial swine enteritis (salmonellosis or necrotic enteritis caused by *Salmonella choleraesuis*);

aid in the prevention of migration and establishment of large roundworm (*Ascaris suum*) infections; aid in the prevention of establishment of nodular worm (*Oesophagostomum*) infections.

(ii) **Limitations.** Do not feed to swine over 75 pounds; do not feed within 10 weeks of slaughter; consult a veterinarian before feeding to severely debilitated animals; feed continuously as sole ration. Do not use in complete feeds containing less than 15 percent crude protein.

[40 FR 13959, Mar. 27, 1975, as amended at 40 FR 45164, Oct. 1, 1975; 40 FR 57798, Dec. 12, 1975; 42 FR 761, Jan. 4, 1977; 51 FR 7396, Mar. 3, 1986]

§ 558.120 Carbarsone (not U.S.P.).

(a) **Approvals.** Type A medicated articles: (1) 37.5 percent to 011794 in § 510.600(c) of this chapter.

(2) 25 percent carbarsone and 5 grams per pound bacitracin (as bacitracin methylene disalicylate) to 011794 in § 510.600(c) of this chapter.

(b) **Related tolerances.** See § 556.60 of this chapter.

(c) **Conditions of use.** (1) It is used for turkeys as follows:

(i) **Grams per ton.** 227 to 340.5 (0.025 to 0.0375 percent).

(a) **Indications for use.** As an aid in the prevention of blackhead.

(b) **Limitations.** Feed continuously beginning 2 weeks before blackhead is expected and continue as long as prevention is needed; withdraw 5 days before slaughter; as sole source of organic arsenic.

(ii) **Grams per ton.** 227 to 340.5 (0.025 to 0.0375 percent) carbarsone plus 10 grams per ton bacitracin from bacitracin methylene disalicylate.

(a) **Indications for use.** As an aid in the prevention of blackhead; for increased rate of weight gain.

(b) **Limitations.** Feed continuously beginning 2 weeks before blackhead is expected and continue as long as prevention is needed; withdraw 5 days before slaughter; as sole source of organic arsenic.

(iii) **Grams per ton.** 227 to 340.5 (0.025 to 0.0375 percent) carbarsone plus 4 to 45 grams per ton bacitracin from bacitracin zinc.

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(a) *Indications for use.* As an aid in the prevention of blackhead, increased rate of weight gain, and improved feed efficiency.

(b) *Limitations.* Feed continuously as sole ration. Withdraw 5 days before slaughter. As sole source of organic arsenic; as bacitracin zinc provided by No. 011716 in § 510.600(c) of this chapter.

(2) Carbarsone (not U.S.P.) may be used in accordance with the provisions of this section in the combinations provided as follows:

(i) Zoalene in accordance with § 558.680.

(ii) Amprolium as in § 558.55.

(iii) Bambermycins as in § 558.95.

[41 FR 10995, Mar. 15, 1976, as amended at 42 FR 18617, Apr. 8, 1977; 46 FR 46797, Sept. 22, 1981; 48 FR 2758, Jan. 21, 1983; 51 FR 7396, Mar. 3, 1986; 52 FR 2687, Jan. 26, 1987; 53 FR 20843, June 7, 1988]

§ 558.128 Chlortetracycline.

(a) *Approvals.* Type A medicated articles: 10 to 100 grams per pound chlortetracycline to 010042 in § 510.600(c) of this chapter; 35 grams chlortetracycline with 7.7 percent (35 grams) sulfamethazine to 010042 in § 510.600(c) of this chapter.

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(b) *Related tolerances.* See of this chapter.

(c) *Conditions of use.* (1) I the feed for cockatoos, ma parrots as follows:

(i) *Amount.* 10 milligrams of finished feed.

(ii) *Indications for use.* Tr psittacine birds (cockatoos and parrots) suspected or kn infected with psittacosis (*Chlamydia psittaci* sensitive tetracycline.

(iii) *Limitations.* Feed con for 45 days. As chlortetracy um complex equivalent to cycline hydrochloride. E should consume daily an a medicated feed equal to one body weight. *Warning:* "F avian chlamydiosis, or ornit reportable communicable transmissible between wild a tic birds, other animals, and tact appropriate public healt ulatory officials."

(2) It is used in the feed for ry mice as follows:

(i) *Amount.* Not less than per ton of feed.

(ii) *Indications for use.* As reducing the incidence of ba arrhea.

(3) It is used in feeds as foll

TABLE 1—IN TYPE C FEED

Chlortetracycline in grams per ton	Combination in grams per ton	Indications for use	Limitations
(i) 10 to 50		1. Chickens and turkeys; growth promotion and feed efficiency. 2. Swine; growth promotion and feed efficiency.	As chlortetracycline hydrochloride. do.....
(ii) 20 to 50		1. Lambs and growing sheep; growth promotion and feed efficiency. 2. Mink; growth promotion and feed efficiency; as an aid in increasing pelt size.	do..... do.....
(iii) 50 to 100		1. Chickens and turkeys; during times of stress, for prevention of diseases named in this section caused by organisms susceptible to the indicated levels of the cycline salt. 2. For chickens; prevention of chronic respiratory disease (air-sac infection). 3. For turkeys; prevention of infectious sinusitis, hexamitiasis.	do..... do..... do.....

TABLE 1—IN TYPE C FEED—Continued

Chlortetracycline in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
(a) 100 to 200		4. For laying chickens; maintaining or increasing egg production or hatchability of eggs.	do	
		5. For chicks; prevention of early mortality due to organisms susceptible to chlortetracycline.	do	
		6. Swine; maintenance of weight gain in the presence of atrophic rhinitis; reduction of the incidence of cervical abscesses; prevention of bacterial swine enteritis; prevention of bacterial swine enteritis during times of stress.	do	
		1. For chickens; treatment of chronic respiratory disease (air-sac infection), blue comb (nonspecific infectious enteritis); prevention of synovitis.	Not to be fed to laying chickens; as chlortetracycline hydrochloride.	
(b) 200		2. For turkeys; treatment of blue comb (nonspecific infectious enteritis, mud fever), infectious sinusitis, hexamitiasis; prevention of synovitis.	As chlortetracycline hydrochloride.	
		3. For chickens; treatment of chronic respiratory disease (air-sac infection), blue comb (nonspecific infectious enteritis); prevention of synovitis.	Not to be fed to laying chickens; as chlortetracycline hydrochloride as follows: In low-calcium feed containing 0.8% dietary calcium, not to be fed continuously for more than 8 weeks; in low-calcium feed containing 0.40% to 0.55% dietary calcium, not to be fed continuously for more than 5 d; in low-calcium feed containing 0.8% dietary calcium and 1% to 1.5% sodium sulfate, to be fed continuously for not more than the first 3 weeks of life.	
		4. Swine; treatment of bacterial swine enteritis.	As chlortetracycline hydrochloride.	
		1. For chickens; prevention and control of coccidiosis caused by <i>Eimeria necatrix</i> and <i>E. tenella</i> .	Not to be fed to laying chickens; as chlortetracycline hydrochloride in low-calcium feed containing 0.8% dietary calcium, not to be fed continuously for more than 8 weeks; in low-calcium feed containing 0.8% dietary calcium and 1.0% to 1.5% sodium sulfate, to be fed continuously for not more than the first 3 weeks of life.	
(c) 200		2. For chickens; treatment of coccidiosis caused by <i>Eimeria necatrix</i> and <i>E. tenella</i> .	Not to be fed to laying chickens; as chlortetracycline hydrochloride in low-calcium feed containing 0.4% to 0.55% dietary calcium, not to be fed continuously for more than 5 d.	
		3. For chickens; control of synovitis.	Not to be fed to laying chickens; as chlortetracycline hydrochloride.	
		4. For turkeys; control of synovitis.	As chlortetracycline hydrochloride.	

TABLE 1—IN TYPE C FEED—Continued

Chlortetracycline in grams per ton	Combination in grams per ton	Indications for use	Limitations
(vi) 200 to 400		5. For broiler chickens; treatment of chronic respiratory disease caused by strains of <i>Mycoplasma gallisepticum</i> susceptible to chlortetracycline. 6. Swine; as an aid in reducing spread of leptospirosis. For ducks; for the control and treatment of fowl cholera caused by <i>Pasteurella multocida</i> susceptible to chlortetracycline.	In low calcium feed containing 0.8% dietary calcium; 1.5% sodium sulfate; continuously as sole feed for not more than the first 4 weeks of life. Sole medication; as chlortetracycline hydrochloride. Feed in complete ration to provide from 8 to 28 mg per pound of body weight per day depending upon age and severity of disease; for more than 21 d; as the calcium complex of chlortetracycline equivalent to chlortetracycline hydrochloride.
(vii) 400		1. For turkey poults not over 4 weeks of age; aid in reducing mortality due to paratyphoid caused by <i>Salmonella typhimurium</i> . 2. Swine; as an aid in reducing shedding of leptospires; as an aid in reducing the abortion rate of swine and the mortality rate of newborn pigs when leptospirosis is present.	In low calcium feed containing 1% total calcium with less than 0.45% calcium from calcium sulfate; chlortetracycline hydrochloride. To be fed for 14 d as medication; as chlortetracycline hydrochloride.
(viii) 500		For chickens; aid in the reduction of mortality due to <i>E. coli</i> infections susceptible to such treatment.	Not to be fed to laying chickens; as chlortetracycline hydrochloride; in feed containing 0.8% dietary calcium; to be fed continuously more than 5 d; withdraw 48 h prior to slaughter.

TABLE 2—IN TYPE B FEED

Chlortetracycline MILLIGRAMS PER POUND OF BODY WEIGHT PER DAY	Combination in milligrams per head per day	Indications for use	Limitations
(i) 0.1		For calves up to 250 lb in weight in milk replacers or starter feeds; growth promotion and feed efficiency.	
(ii) 0.5		1. For beef cattle over 1,500 lb in weight; aid in prevention of anaplasmosis. 2. For calves up to 250 lb in weight; aid in the prevention of bacterial diarrhea.	Not to be administered within 48 h of slaughter. In milk replacers or starter feeds.

TABLE 2—IN TYPE B FEED—Continued

Chlortetracycline	Combination in milligrams per head per day	Indications for use	Limitations	Sponsor
(a) 5.0		For beef cattle; aid in the elimination of the carrier state of anaplasmosis.	Feed for 60 days; for use in the carrier state only; not to be fed within 10 d of slaughter. Labeling shall include a statement that a positive complement-fixation test at conclusion of a 60-d feeding period does not necessarily establish that anaplasmosis carrier state is still active. To positively establish that the carrier state has been eliminated, inject blood from a suspected carrier into a splenectomized (susceptible) calf.	
MILLIGRAMS PER HEAD PER DAY				
(a) 25 to 70		For calves in finished feed; growth promotion and feed efficiency.		
(a) 70		1. For feedlot cattle; aid in prevention of liver abscesses. 2. For beef cattle up to 700 lb in weight; aid in reduction of bacterial diarrhea; aid in prevention of foot rot. 3. For growing cattle in finished feed; growth promotion and feed efficiency.		
(a) 85		For horses up to 1 yr of age; growth promotion and feed efficiency.	Do not slaughter for food purposes.	
(a) 100		For beef cattle over 700 lb in weight; aid in reduction of bacterial diarrhea; aid in prevention of foot rot.		
(a) 350		1. For beef cattle; aid in prevention of bacterial pneumonia and shipping fever (hemorrhagic septicemia); aid in reduction of losses due to respiratory infection (infectious rhinotracheitis, shipping fever complex). 2. For beef cattle up to 700 lb in weight; aid in prevention of anaplasmosis.	Not to be administered within 48 h of slaughter.	
	Sulfamethazine 350	For beef cattle; aid in the maintenance of weight gains in the presence of respiratory disease such as shipping fever.	Not to be administered within 48 h of slaughter.	
(a) 500		For beef cattle 700 to 1,000 lb in weight; aid in prevention of anaplasmosis.	Not to be administered within 48 h of slaughter.	
(a) 750		For beef cattle 1,000 to 1,500 lb in weight; aid in prevention of anaplasmosis.	do	

(4) It is used in free-choice cattle feeds such as feed blocks or salt-mineral mixes manufactured from approve Type A articles; such feeds are given to beef cattle and nonlactating dairy

cattle to provide a daily minimum intake of 0.5 milligram of chlortetracycline per pound of body weight to aid in the prevention of anaplasmosis; the use of these Type A articles to make

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specific free-choice feed formulations must be approved under section 512(b) of the act and be based on a demonstration of drug stability and consumption which is consistent with the effective dose; the specific free-choice feed formulations approved in this paragraph can be manufactured under section 512(m) of the act.

(5) Chlortetracycline may be used in accordance with the provisions of this section in the combinations provided as follows:

(i) Amprolium in accordance with § 558.55.

(ii) Amprolium plus ethopabate in accordance with § 558.58.

(iii) Buquinolate in accordance with § 558.105.

(iv) Clopidol in accordance with § 558.175.

(v) Decoquinat in accordance with § 558.195.

(vi) [Reserved]

(vii) Hygromycin B in accordance with § 558.274.

(viii) Monensin in accordance with § 558.355.

(ix) Robenidine hydrochloride in accordance with § 558.515.

(x) Roxarsone in accordance with § 558.530.

(xi) Zoalene in accordance with § 558.680.

[41 FR 10995, Mar. 15, 1976, as amended at 42 FR 18617, Apr. 8, 1977; 42 FR 36995, July 19, 1977; 47 FR 9399, Mar. 5, 1982; 47 FR 51563, Nov. 16, 1982; 48 FR 11429, Mar. 18, 1983; 51 FR 7396, Mar. 3, 1986; 52 FR 2684, Jan. 26, 1987; 53 FR 31316, Aug. 18, 1988]

§ 558.145 Chlortetracycline, procaine penicillin, and sulfamethazine.

(a) *Approvals.* Type A medicated articles: (1) 20 grams of chlortetracycline per pound, 4.4 percent (20 grams) of sulfamethazine, and procaine penicillin equivalent in activity to 10 grams of penicillin per pound to 000069 and 010042 in § 510.600(c) of this chapter.

(2) 40 grams of chlortetracycline per pound, 8.8 percent of sulfamethazine, and penicillin procaine equivalent in activity to 20 grams of penicillin per pound to 010042 in § 510.600(c) of this chapter.

(b) *Specifications.* (1) The antibiotic substance refers to the antibiotic or feed-grade antibiotic.

(2) The antibiotic activities are expressed in terms of the appropriate antibiotic standards.

(3) Type C medicated feed contains in each ton, 100 grams of chlortetracycline, 50 grams of penicillin as procaine penicillin, and 100 grams of sulfamethazine.

(c) *Related tolerances.* See §§ 556.150, 556.510, and 556.670 of this chapter.

(d) *Conditions of use.* (1) It is administered to swine in a Type C feed for reduction of the incidence of cervical abscesses; treatment of bacterial swine enteritis (salmonellosis or necrotic enteritis caused by *Salmonella choleraesuis* and vibronic dysentery); prevention of these diseases during times of stress; maintenance of weight gains in the presence of atrophic rhinitis; growth promotion and increased feed efficiency in swine weighing up to 75 pounds.

(2) Withdraw 15 days prior to slaughter.

[40 FR 13959, Mar. 27, 1975, as amended at 43 FR 19385, May 5, 1978; 47 FR 39814, Sept. 10, 1982; 48 FR 30615, July 5, 1983; 51 FR 7396, Mar. 3, 1986; 52 FR 2684, Jan. 26, 1987]

§ 558.155 Chlortetracycline, procaine penicillin, and sulfathiazole.

(a) *Approvals.* Type A medicated articles: (1) 20 grams of chlortetracycline hydrochloride, 4.4 percent (20 grams) sulfathiazole, and procaine penicillin equivalent to 10 grams of penicillin per pound to 054273 in § 510.600(c) of this chapter.

(2) 40 grams of chlortetracycline hydrochloride, 8.8 percent (40 grams) sulfathiazole and procaine penicillin equivalent in activity to 20 grams of penicillin per pound to 054273 in § 510.600(c) of this chapter.

(b) *Specifications.* (1) The antibiotic substance refers to the antibiotic or feed-grade antibiotic.

(2) The antibiotic activities are expressed in terms of the appropriate antibiotic standards.

(c) *Related tolerances.* See §§ 556.150, 556.510, and 556.690 of this chapter.

(d) *Conditions of use.* It is used for swine as follows:

- (1) Amount per ton. Chlortetracycline, 100 grams plus penicillin, 50 grams plus sulfathiazole, 100 grams.
- (2) Indications for use. For increased rate of weight gain and improved feed efficiency in animals up to 6 weeks postweaning. For increased rate of weight gain in animals from 6 to 16 weeks postweaning. Maintenance of weight gains in the presence of atrophic rhinitis; reduction of the incidence of cervical abscesses; treatment of bacterial swine enteritis (salmonellosis or necrotic enteritis caused by *Salmonella choleraesuis* and vibronic dysentery).
- (3) Limitations. For swine raised in confinement (dry-lot) or on limited pasture; withdraw 7 days prior to slaughter; as procaine penicillin and chlortetracycline hydrochloride, as follows:

MINIMUM AMOUNT OF TYPE C FEED WHICH THE ANIMAL SHOULD CONSUME

Type of feed	Approximate body weight in pounds	Minimum desired daily feed intake in pounds
Prestarter (up to 6 weeks postweaning)	20	1
Starter (up to 6 weeks postweaning)	50	1 1/2
Grower (6-16 weeks postweaning)	80	2
Finisher (6-16 weeks postweaning)	150	3

40 FR 13959, Mar. 27, 1975, as amended at 51 FR 7397, Mar. 3, 1986; 51 FR 28547, Aug. 1986; 52 FR 2684, Jan. 26, 1987

558.175 Clopidol.

- (a) Approvals. Type A medicated articles: (1) 25 percent to 011526 in § 510.600(c) of this chapter.
- (2) 25 percent of clopidol, 10 percent of roxarsone, and 4, 10, 15, or 25 grams of bacitracin methylene disalicylate per pound to 011526 in § 510.600(c) of this chapter.
- (b) Related tolerances. See § 556.160 of this chapter.
- (c) Conditions of use. It is used as follows:
 - (1) Broiler chickens—(i) Amount per ton. Clopidol 113.5 grams (0.0125 percent).

- (a) Indications for use. Aid in the prevention of coccidiosis caused by *E. tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*.
- (b) Limitations. Do not feed to chickens over 16 weeks of age.
- (ii) Amount per ton. Clopidol, 113.5 grams (0.0125 percent) plus roxarsone, 45.4 grams (0.005 percent).
- (a) Indications for use. Aid in the prevention of coccidiosis caused by *E. tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*; growth promotion and feed efficiency; improved pigmentation.
- (b) Limitations. Do not feed to chickens over 16 weeks of age; withdraw 5 days before slaughter; as sole source of organic arsenic.
- (iii) Amount per ton. Clopidol, 113.5 grams (0.0125 percent) plus roxarsone, 45.4 grams (0.005 percent) plus bacitracin, 4-25 grams.
- (a) Indications for use. Aid in the prevention of coccidiosis caused by *E. tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*; growth promotion and feed efficiency; improved pigmentation; increased rate of weight gain.
- (b) Limitations. Do not feed to chickens over 16 weeks of age; withdraw 5 days before slaughter; as sole source of organic arsenic; as bacitracin methylene disalicylate, provided by No. 046573 in § 510.600(c) of this chapter; or as zinc bacitracin provided by No. 011716 in § 510.600(c) of this chapter.

- (iv) Amount per ton. Clopidol, 113.5 grams (0.0125%) plus zinc bacitracin, 5 to 25 grams.
- (a) Indications for use. For increased rate of weight gain and improved feed efficiency; aid in the prevention of coccidiosis caused by *E. tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*.
- (b) Limitations. Feed continuously as sole ration. Zinc bacitracin as provided by No. 011716 of § 510.600(c) of this chapter.
- (v) Amount per ton. Clopidol, 113.5 grams (0.0125 percent) plus bacitracin methylene disalicylate, 4 to 50 grams per ton.
- (a) Indications for use. For increased rate of weight gain; to aid in the prevention of coccidiosis caused by

E. tenella, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. mivati*, and *E. brunetti*.

(b) *Limitations*. Feed continuously as the sole ration from the time chicks are placed in floor pens until slaughter. Do not feed to chickens over 16 weeks of age. Bacitracin methylene disalicylate as provided by No. 046573 in § 510.600(c) of this chapter.

(vi) *Amount per ton*. Clopidol, 113.5 grams (0.0125 percent) plus lincomycin, 2-4 grams.

(a) *Indications for use*. Aid in the prevention of coccidiosis caused by *E. tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*; increase in rate of weight gain and improved feed efficiency.

(b) *Limitations*. As lincomycin hydrochloride monohydrate; do not feed to chickens over 16 weeks of age.

(2) *Broiler chickens and replacement chickens*—(i) *Amount per ton*. Clopidol, 113.5 or 227 grams (0.0125 or 0.025 percent).

(a) *Indications for use*. Aid in the prevention of coccidiosis caused by *E. tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*.

(b) *Limitations*. Feed up to 16 weeks of age if intended for use as caged layers; feed continuously as the sole ration; withdraw 5 days before slaughter if given at the level of 0.025 percent in feed or reduce level to 0.0125 percent 5 days before slaughter.

(ii) *Amount per ton*. 113.5 grams (0.0125 percent) clopidol with 200 grams chlortetracycline.

(a) *Indications for use*. Aid in the prevention of coccidiosis caused by *E. tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. mivati*, and *E. brunetti*, and infectious synovitis caused by *Mycoplasma synoviae*.

(b) *Limitations*. Feed continuously as sole ration from the time chicks are placed in floor pens, up to 21 days of age.

(3) [Reserved]

(4) *Replacement chickens*—(i) *Amount per ton*. Clopidol 113.5 grams (0.0125 percent).

(a) *Indications for use*. Aid in the prevention of coccidiosis caused by *E. tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*.

(b) *Limitations*. For replacement chickens intended for use as caged

layers; do not feed to chickens over 16 weeks of age.

(ii) *Amount per ton*. Clopidol 113.5 grams (0.0125 percent) plus roxarsone 45.4 grams (0.005 percent).

(a) *Indications for use*. Aid in the prevention of coccidiosis caused by *E. tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*; growth promotion and feed efficiency; improving pigmentation.

(b) *Limitations*. For replacement chickens intended for use as caged layers; do not feed to chickens over 16 weeks of age; withdraw 5 days before slaughter; as sole source of organic arsenic.

(5) *Turkeys*—(i) *Amount per ton*. Clopidol 113.5 or 227 grams (0.0125 or 0.025 percent).

(ii) *Indications for use*. Aid in the prevention of leucocytozoonosis caused by *Leucocytozoon smithi*.

(iii) *Limitations*. For turkeys grown for meat purposes only; to be administered continuously in feed at 0.0125 or 0.025 percent clopidol as the sole ration depending upon management practices, degree of exposure, and amount of feed eaten; withdraw medication 5 days before slaughter.

[40 FR 13959, Mar. 27, 1975, as amended at 40 FR 31935, July 30, 1975; 40 FR 52721, Nov. 12, 1975; 41 FR 1062, Jan. 6, 1976; 41 FR 53002, Dec. 3, 1976; 44 FR 20676, Apr. 6, 1979; 51 FR 7397, Mar. 3, 1986; 52 FR 2684, Jan. 26, 1987; 53 FR 20843, June 7, 1988; 54 FR 6518, Feb. 13, 1989]

§ 558.185 Coumaphos.

(a) *Approvals*. Type A medicated articles: (1) 1.12, 2.0, 11.2, and 50 percent to 000859 in § 510.600(c) of this chapter for use as in paragraph (d) of this section.

(2) 1.12 and 11.2 percent to 017800 in § 510.600(c) of this chapter for use as in paragraph (d)(1)(ii) of this section.

(b) *Special considerations*. Adequate directions and warnings for use must be given and shall include a statement that coumaphos is a cholinesterase inhibitor and that animals being treated with coumaphos should not be exposed during or within a few days before or after treatment to any other cholinesterase-inhibiting drugs, insecticides, pesticides, or chemicals.

(c) *Related tolerances.* See 40 CFR 180.189.

(d) *Conditions of use.* It is used as follows:

(1) *Beef and dairy cattle*—(i) *Amount.* Coumaphos 0.00012 lb. (0.054 gram) per 100 lb. body weight per day.

(a) *Indications for use.* As an aid in the reduction of fecal breeding flies through control of fly larvae.

(b) *Limitations.* Feed for the duration of fly season in a Type C feed containing 0.0033 percent or in a feed Type B feed containing not over 0.0066 percent coumaphos; do not feed to animals less than 3 months old; not for use in pelleted feeds.

(ii) *Amount.* Coumaphos, 0.0002 lb. (0.091 gram) per 100 lb. body weight per day.

(a) *Indications for use.* Control of gastrointestinal roundworms (*Haemonchus* spp., *Ostertagia* spp., *Cooperia* spp., *Nematodirus* spp., *Trichostrongylus* spp.).

(b) *Limitations.* Feed 0.0002 lb. (0.091 gram) per 100 lb. body weight per day for 6 consecutive days in the normal grain ration to which the animals are accustomed but not in rations containing more than 0.1 percent coumaphos; do not feed to animals less than 3 months old; do not feed to sick animals or animals under stress, such as those just shipped, dehorned, castrated, or weaned within the last 3 weeks; do not feed in conjunction with anthelmintic drenches or with feeds containing penothiazine. Should conditions warrant, repeat treatment at 30-day intervals.

(3) *Laying chickens*—(i) *Amount.* Coumaphos 27.2 grams per ton (0.003 percent).

(ii) *Indications for use.* For control of capillary worm (*Capillaria obsignata*) and as an aid in control of common round worm (*Ascaridia galli*) and cecal worm (*Heterakis gallinae*).

(iii) *Limitations.* In Type C feed; administer continuously as the total feed ration for 14 days; when reinfection occurs, treatment may be repeated but not sooner than 3 weeks after the end of the previous treatment; do not feed to chickens within 10 days of vaccination or other conditions of stress; treatment of colored breeds of commercial layers should be avoided while

in production since these breeds appear to be more sensitive to coumaphos than white breeds; as sole medication; medications in general should be avoided while birds are approaching peak production; such interruption of normal feeding practices may upset the flock and lower egg production; diagnosis by competent personnel is essential; flock condition and production records should be carefully evaluated prior to treatment.

(3) *Replacement pullets*—(i) *Amount.* Coumaphos 36.3 grams per ton (0.004 percent).

(ii) *Indications for use.* For control of capillary worm (*Capillaria obsignata*) and as an aid in control of common roundworm (*Ascaridia galli*) and cecal worm (*Heterakis gallinae*).

(iii) *Limitations.* In Type C feed; administer before the onset of production; diagnosis by competent personnel is essential; administer continuously as total feed ration for from 10 to 14 days; do not feed to chickens under 8 weeks of age nor within 10 days of vaccination or other conditions of stress; if birds are maintained on contaminated litter or exposed to infected birds, a second 10 to 14 day treatment is recommended but not sooner than 3 weeks after the end of the previous treatment; as sole medication; if reinfection occurs after production begins, repeat treatment as recommended for laying flocks.

[40 FR 13959, Mar. 27, 1975, as amended at 42 FR 1463, Jan. 7, 1977; 51 FR 7397, Mar. 3, 1986; 52 FR 2684, Jan. 26, 1987]

§ 558.195 Decoquinat.

(a) *Approvals.* Type A medicated articles: 6 percent to 011526 in § 510.600(c) of this chapter.

(b) *Related tolerances in edible products.* See § 556.170 of this chapter.

(c) *Special considerations.* (1) Bentonite should not be used in decoquinat feeds.

(2) Complete broiler feeds and complete or supplemental cattle feeds containing decoquinat as the sole drug, processed from premixes containing 6 percent decoquinat and conforming to the requirements of paragraphs (g) (1) and (2) of this section, are not re-

quired to comply with the provisions of section 512(m) of the Act.

(3) Type A medicated articles containing 6 percent decoquinatate may be used to manufacture dry or liquid

Type B cattle feeds as indicated in paragraph (d) of this section.

(d) *Conditions of use.* It is used as follows:

Decoquinatate in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
27.2 (0.003 pct.)		Broiler chickens; for the prevention of coccidiosis caused by <i>Eimeria tenella</i> , <i>E. necatrix</i> , <i>E. mivati</i> , <i>E. acervulina</i> , <i>E. maxima</i> and <i>E. brunetti</i> .	Do not feed to laying chickens.	011528
	Bacitracin 10 to 50	Broiler chickens; for the prevention of coccidiosis caused by <i>Eimeria tenella</i> , <i>E. necatrix</i> , <i>E. mivati</i> , <i>E. acervulina</i> , <i>E. maxima</i> , and <i>E. brunetti</i> ; for increased rate of weight gain and improved feed efficiency.	Do not feed to laying chickens; feed as sole ration; as zinc bacitracin provided by No. 011716 in sec. 510.600(c) of this chapter.	011528
	Chlortetracycline 200	Broiler chickens; for the prevention of coccidiosis caused by <i>Eimeria tenella</i> , <i>E. necatrix</i> , <i>E. acervulina</i> , <i>E. mivati</i> , <i>E. maxima</i> , and <i>E. brunetti</i> ; for the treatment of chronic respiratory disease (air-sac infection), prevention of synovitis.	Do not feed to laying chickens; in low calcium feed containing 0.8 pct. of calcium; not to be fed continuously for more than 8 weeks; as chlortetracycline hydrochloride provided by No. 010042 in sec. 510.600(c) of this chapter.	011528
	Roxarsone 45.4 (0.005 pct.)	Broiler chickens; for the prevention of coccidiosis caused by <i>Eimeria tenella</i> , <i>E. necatrix</i> , <i>E. mivati</i> , <i>E. acervulina</i> , <i>E. maxima</i> , and <i>E. brunetti</i> ; growth promotion and feed efficiency; improving pigmentation.	Do not feed to laying chickens; withdraw 5 days before slaughter; as sole source of organic arsenic.	011528
	Lincomycin 2	Broiler chickens; for the prevention of coccidiosis caused by <i>Eimeria tenella</i> , <i>E. necatrix</i> , <i>E. acervulina</i> , <i>E. maxima</i> , <i>E. mivati</i> , and <i>E. brunetti</i> ; for increased rate of weight gain and improved feed efficiency.	Do not feed to laying chickens; feed as sole ration; as lincomycin hydrochloride monohydrate provided by No. 000009 in sec. 510.600(c) of this chapter.	000000, 011528
	Roxarsone 11 to 45 (0.0012-0.005 pct.) plus Bacitracin 12 to 50.	Broiler chickens; for the prevention of coccidiosis caused by <i>Eimeria tenella</i> , <i>E. necatrix</i> , <i>E. acervulina</i> , <i>E. mivati</i> , <i>E. maxima</i> , and <i>E. brunetti</i> ; for increased rate of weight gain and improved feed efficiency.	Do not feed to laying chickens; withdraw 5 days before slaughter; as sole source of organic arsenic; as zinc bacitracin provided by No. 011716 in sec. 510.600(c) of this chapter; as roxarsone provided by No. 017210 in sec. 510.600(c) of this chapter.	011528

Decoquinat in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
22.7 mg per 100 lb of body weight per day (0.5 mg per kilogram).		Cattle; for the prevention of coccidiosis in ruminating calves and cattle caused by <i>Eimeria bovis</i> and <i>E. zurni</i> .	Administer as a Type C feed containing 0.0015 pct to 0.003 pct decoquinat, as a dry Type B feed containing 0.05 pct to 0.5 pct decoquinat, or as a liquid Type B feed containing 0.0125 pct to 0.05 pct decoquinat. The liquid Type B feed to be used must have a pH range of 5.0 to 6.5 and contain a suspending agent to maintain a viscosity of not less than 500 centipoises. Feed at least 28 days during periods of exposure to coccidiosis or when it is likely to be a hazard. Do not feed to cows producing milk for food.	
13.6 (0.00149 pct).		Young goats; for the prevention of coccidiosis caused by <i>Eimeria christensenii</i> and <i>E. ninakohlyakimovae</i> .	Feed at a rate to provide 22.7 mg per 100 lbs of body weight per day (0.5 mg per kilogram); do not feed to goats producing milk for food; feed for at least 28 days during periods of exposure to coccidiosis or when it is likely to be a hazard.	011526

140 FR 13959, Mar. 27, 1975, as amended at 41 FR 53003, Dec. 3, 1976; 42 FR 2312, Jan. 11, 1977; 43 FR 32750, July 28, 1978; 44 FR 20676, Apr. 6, 1979; 45 FR 62426, Sept. 19, 1980; 46 FR 32019, June 19, 1981; 51 FR 7397, Mar. 3, 1986; 51 FR 34589, Sept. 30, 1986; 52 FR 2684, Jan. 26, 1987; 52 FR 4992, Feb. 18, 1987; 52 FR 38924, Oct. 20, 1987; 52 FR 43061, 43062, Nov. 9, 1987; 53 FR 20843, June 7, 1988; 53 FR 22298, June 15, 1988; 54 FR 11183, Mar. 17, 1989

§ 558.205 Dichlorvos.

(a) **Approvals.** Type A medicated articles; 3.1 and 9.6 percent to 054273 in 510.600(c) of this chapter.

(b) **Special considerations.** (1) Dichlorvos is to be included in meal or mash or mixed with feed in crumble form only after the crumble feed has been manufactured. Do not mix in feeds to be pelleted nor with pelleted feed. Do not soak the feed or administer as wet mash. Feed must be dry when administered. Do not use in animals other than swine. Do not allow owl access to feed containing this preparation or to feces from treated animals.

(2) Dichlorvos is a cholinesterase inhibitor. Do not use this product in animals simultaneously or within a few days before or after treatment with or exposure to cholinesterase-inhibiting drugs, pesticides, or chemicals. If human or animal poisoning should occur, immediately consult a physician

or a veterinarian. Atropine is antidotal.

(3) **Labeling for Type A articles and Type B feeds** must include a statement that containers or materials used in packaging such Type A articles and Type B feeds are not to be reused and all such packaging materials must be destroyed after the product has been used.

(c) **Related tolerances.** See § 556.180 of this chapter.

(d) **Conditions of use.** It is used in feed for swine as follows:

(1) **Amount per ton.** Dichlorvos, 348 grams (0.0384 percent).

(i) **Indications for use.** For the removal and control of mature, immature, and/or fourth-stage larvae of the whipworm (*Trichuris suis*), nodular worm (*Oesophagostomum sp.*), large roundworm (*Ascaris suum*) and the thick stomach worm (*Ascarops strongylina*) of the gastrointestinal tract.

(ii) **Limitations.** For swine up to 70 pounds body weight, feed as sole

ration for 2 consecutive days. For swine from 70 pounds to market weight, feed as sole ration at the rate of 8.4 pounds of feed per head until the medicated feed has been consumed. For boars, open or bred gilts, and sows, feed as sole ration at the rate of 4.2 pounds per head per day for 2 consecutive days.

(2) *Amount per ton.* Dichlorvos, 479 grams (0.0528 percent).

(i) *Indications for use.* For the removal and control of mature, immature, and/or fourth-stage larvae of the whipworm (*Trichuris suis*), nodular worm (*Oesophagostomum* sp.), large roundworm (*Ascaris suum*), and the thick stomach worm (*Ascarops strongylina*) of the gastrointestinal tract.

(ii) *Limitations.* For boars, open or bred gilts, and sows, feed as sole ration at the rate of 6 pounds per head for one feeding.

(3) *Amount per ton.* Dichlorvos, 334-500 grams (0.0366-0.0550 percent).

(i) *Indications for use.* An aid in improving litter production efficiency by increasing pigs born alive, birth weights, survival to market, and rate of weight gain. Treatment also removes and controls mature, immature and/or fourth stage larvae of whipworm (*Trichuris suis*), nodular worm

(*Oesophagostomum* spp.) large roundworm (*Ascaris suum*), and the thick stomach worm (*Ascarops strongylina*) occurring in the gastrointestinal tract of the sow or gilt.

(ii) *Limitations.* For pregnant swine, mix into a gestation feed to provide 1,000 milligrams per head daily during last 30 days of gestation.

[40 FR 13959, Mar. 27, 1975, as amended at 40 FR 50258, Oct. 29, 1975; 46 FR 48815, Oct. 13, 1983; 51 FR 7397, Mar. 3, 1986; 51 FR 28547, Aug. 8, 1986; 52 FR 2684, Jan. 20, 1987]

§ 558.248 Erythromycin thiocyanate.

(a) *Approvals.* Type A medicated articles: (1) 2.2 percent to 050604 in § 510.600(c) of this chapter for use as in paragraph (d) of this section.

(2) 5 and 10 percent to 050604 for use in paragraphs (d)(1)(i) and (ii) of this section.

(b) *Special considerations.* The levels of antibiotic are expressed in terms of erythromycin master standard. One gram of erythromycin thiocyanate is equivalent to 0.925 gram of erythromycin master standard.

(c) *Related tolerances.* See § 556.230 of this chapter.

(d) *Condition of use.* (1) It is used as follows:

Erythromycin thiocyanate in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
(i) 4.6 to 18.5		Chickens; growth promotion and feed efficiency.		050604
(ii) 9.25 to 18.5		Turkeys; growth promotion and feed efficiency.	For turkeys not over 12 weeks of age.	050604
(iii) 9.25 to 64.75		Swine; increase in weight gain, improved feed efficiency in starter pigs (9.25 to 64.75) and grower-finishing pigs (9.25).	Starter ration for animals up to 35 lb body weight.	050604
(iv) 18.5		Laying chickens; aids in increasing egg production. 2. Chickens; as an aid in the prevention of infectious coryza. 3. Turkeys; as an aid in the prevention of chronic respiratory disease during periods of stress.	Feed for 7 to 14 d; withdraw 24 h before slaughter. Feed for 2 d before stress and 3 to 6 d after stress.	050604
(v) 92.5		1. Chickens; as an aid in the prevention of chronic respiratory disease during periods of stress.	Feed for 2 d before stress and 3 to 6 d after stress; withdraw 24 h before slaughter.	050604
(vi) 185		1. Chickens; as an aid in the prevention and reduction of lesions and in lowering severity of chronic respiratory disease.	Feed for 5 to 8 d; do not use in birds producing eggs for food purposes; withdraw 48 h before slaughter.	050604

Erythromycin thiocyanate in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
		2. Turkeys; as an aid in the prevention and reduction of lesions and in lowering severity of chronic respiratory disease.	Feed for 5 to 8 d; do not use in birds producing eggs for food purposes.	050604

(2) In feed for feedlot beef cattle at 7 milligrams per head per day as an aid in stimulating growth and improving feed efficiency.

(3) Erythromycin thiocyanate may be used in accordance with the provisions of this section in the combinations provided as follows:

(i) Amprolium in accordance with § 558.55.

(ii) Amprolium and ethopabate in accordance with § 558.58.

(iii) Arsanilic acid in accordance with § 558.62.

(iv) Zoalene in accordance with § 558.60.

1 FR 10999, Mar. 15, 1976, as amended at FR 56799, Aug. 26, 1980; 49 FR 31281, Aug. 6, 1984; 51 FR 7397, Mar. 3, 1986; 52 FR 2684, Jan. 26, 1987; 54 FR 12189, Mar. 1989)

EFFECTIVE DATE NOTE: At 54 FR 12189, Mar. 24, 1989, (a) (3), (4), and (5) were re-

moved, and in the table in paragraph (d)(1), the sponsor number "000004" was removed from the last column in the entries for (i), (ii), and (v), effective April 3, 1989. For the convenience of the user, the text in effect until April 3, 1989 follows.

§ 558.248 Erythromycin thiocyanate.

* * * * *

(a) * * *

(3) 3.7 grams per pound to 000004 for use as in paragraphs (d)(1)(i) and (ii) of this section.

(4) 9.25 grams per pound to 000004 for use as in paragraph (d)(1)(v), item 3 of this section.

(5) 18.5 grams per pound to 000004 for use as in paragraph (d)(1)(v), item 1 of this section.

* * * * *

(d)(1)

Erythromycin thiocyanate in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
0 to 18.5		Chickens; growth promotion and feed efficiency.		000004, 050604
18.5 to 18.5		Turkeys; growth promotion and feed efficiency.	For turkeys not over 12 weeks of age.	000004, 050604
18.5		1. Chickens; as an aid in the prevention of chronic respiratory disease during periods of stress.	Feed for 2 d before stress and 3 to 6 d after stress; withdraw 24 h before slaughter.	000004, 050604

* * * * *

§ 558.254 Famphur.

(a) *Approvals.* Type A medicated articles: 13.2 and 33.3 percent to 010042 and 510.600(c) of this chapter.

(b) *Special considerations.* Famphur is a cholinesterase inhibitor. Do not use this product in animals simultaneously or within a few days before or after treatment with or exposure to

cholinesterase-inhibiting drugs, pesticides, or chemicals.

(c) *Related tolerances.* See 40 CFR 180.233.

(d) *Conditions of use.* It is used in the feed for cattle as follows:

(1) *Amount.* 1.1 milligrams per pound body weight per day.

(i) *Indications for use.* For control of grubs and as an aid in control of sucking lice.

(ii) *Limitations.* For beef cattle and nonlactating dairy cows; feed for 30 days; withdraw from dry dairy cows and heifers 21 days prior to freshening; withdraw 4 days prior to slaughter.

(2) *Amount.* 2.3 milligrams per pound body weight per day.

(i) *Indications for use.* For control of grubs.

(ii) *Limitations.* For beef cattle and nonlactating dairy cows; feed for 10 days; withdraw from dry dairy cows and heifers 21 days prior to freshening; withdraw 4 days prior to slaughter.

[41 FR 11000, Mar. 15, 1976, as amended at 51 FR 7397, Mar. 3, 1986]

§ 558.258 Fenbendazole.

(a) *Approvals.* Type A medicated articles: 4 percent (18.1 grams per pound) fenbendazole and 20 percent (90.7 grams per pound) fenbendazole to 012799 in § 510.600(c) of this chapter.

(b) *Related tolerances.* See § 556.275 of this chapter.

(c) *Conditions of use.* (1) It is used in swine feed as follows:

(i) A total of 9 milligrams per kilogram of body weight given over a 3- to 12-day period for the removal of the adult stage of the large roundworm (*Ascaris suum*), whipworm (*Trichuris suis*), nodular worm (*Oesophagostomum dentatum*, *O. quadrispinulatum*), small stomach worm (*Hyostrongylus rubidus*), lungworm (*Metastrongylus apri* and *M. pulehodotectus*), and the adult and larval stages of the kidneyworm (*Stephanurus dentatus*).

(ii) A total of 9 milligrams per kilogram of body weight given over a 3-day period for removal and control of larvae (L3,4 stages—liver, lung, intestinal forms) of the large roundworm (*A. suum*), and larvae (L2,3,4 stages—intestinal mucosal forms) of the whipworm (*T. suis*).

(iii) Feed as sole ration.

(2) It is used in cattle feed as follows:

(i) *Amount.* 5 milligrams fenbendazole per kilogram body weight (2.27 milligrams per pound).

(ii) *Indications for use.* For the removal and control of lungworms (*Dictyocaulus viviparus*); barberpole worms (*Haemonchus contortus*);

brown stomach worms (*Ostertagia circumcincta*); small stomach worms (*Trichostrongylus axei*); hookworms (*Bunostomum phlebotomum*); thread-necked intestinal worms (*Nematodirus helvetianus*); small intestinal worms (*Cooperia punctata* and *C. oncophora*), bankrupt worms (*Trichostrongylus colubriformis*); and nodular worms (*Oesophagostomum radiatum*).

(iii) *Limitations.* Feed as sole ration for one day. Do not use within 13 days of slaughter. Do not use in dairy cattle of breeding age.

[49 FR 3846, Jan. 31, 1984, as amended at 51 FR 7397, Mar. 3, 1986; 53 FR 14788, Apr. 20, 1988; 53 FR 48533, Dec. 1, 1988]

§ 558.262 Furazolidone.

(a) *Approvals.* Type A medicated articles: 10, 50, and 100 grams per pound to 000007 in 011801 in § 510.600(c) of this chapter.

(b) *Related tolerances.* See § 556.290 of this chapter.

(c) *Conditions of use.* It is used in the feed for swine as follows:

(1) *Amount per ton.* 150 grams (0.0165 percent).

(i) *Indications for use.* In sows, for prevention of bacterial scours in baby pigs; growth promotion while on medication.

(ii) *Limitations.* Feed 1 week before farrowing and 2 weeks after farrowing.

(2) *Amount per ton.* 100 to 200 grams (0.011 to 0.022 percent).

(i) *Indications of use.* Prevention of bacterial enteritis (necrotic enteritis, necro) and vibronic (bloody) dysentery; growth promotion while on medication.

(ii) *Limitations.* Feed 100 grams per ton for 5 weeks; or 150 grams per ton for 3 weeks; or 200 grams per ton for 2 weeks.

(3) *Amount per ton.* 300 grams (0.033 percent).

(i) *Indications for use.* Treatment of bacterial enteritis (necrotic enteritis, necro) and vibronic (bloody) dysentery; growth promotion while on medication.

(ii) *Limitations.* Feed 10 to 14 days.

[41 FR 11000, Mar. 15, 1976, as amended at 51 FR 7397, Mar. 3, 1986]

§ 558.265 Halofuginone hydrobromide.

(a) *Approvals.* Type A medicated articles: 6 grams per kilogram (2.72 grams per pound) to 012579 in § 510.600(c) of this chapter.

(b) *Related tolerances.* See § 556.308 of this chapter.

(c) *Conditions of use.* It is used in feed for broiler chickens as follows:

(1) *Amount.* 2.72 grams per ton.

(i) *Indications for use.* For the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*.

(ii) *Limitations.* Feed continuously as sole ration; withdraw 4 days before slaughter; do not feed to layers; avoid contact with skin, eyes, or clothing; keep out of lakes, ponds, or streams.

(2) *Amount per ton.* Halofuginone 2.72 grams (0.0003 percent) plus bambermycins 1 to 2 grams.

(i) *Indications for use.* For the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*; for increased rate of weight gain and improved feed efficiency.

(ii) *Limitations.* Feed continuously as sole ration; withdraw 5 days before slaughter; do not feed to layers.

(3) *Amount per ton.* Halofuginone 2.72 grams (0.0003 percent) plus virginiamycin 5 grams.

(i) *Indications for use.* For the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*; for increased rate of weight gain and improved feed efficiency.

(ii) *Limitations.* Feed continuously as sole ration; withdraw 6 days before slaughter; do not feed to layers.

(4) *Amount per ton.* Halofuginone 2.72 grams (0.0003 percent) plus virginiamycin 5 to 15 grams.

(i) *Indications for use.* For the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*; for increased rate of weight gain.

(ii) *Limitations.* Feed continuously as sole ration; withdraw 6 days before slaughter; do not feed to layers.

(5) *Amount per ton.* Halofuginone hydrobromide 2.72 grams (0.0003 percent) plus bacitracin methylene dis-

alicylate 10 to 50 grams and roxarsone 22.7 to 45.4 grams.

(i) *Indications for use.* For the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*; for increased rate of weight gain; and for improved feed efficiency.

(ii) *Limitations.* Feed continuously as sole ration; withdraw 5 days before slaughter; use as sole source of organic arsenic; do not feed to layers; avoid contact with skin, eyes, or clothing; keep out of lakes, ponds, or streams.

(6) *Amount per ton.* Halofuginone 2.72 grams (0.0003 percent) plus bacitracin methylene disalicylate 10 to 50 grams.

(i) *Indications for use.* For the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima* and improved feed efficiency.

(ii) *Limitations.* Feed continuously as sole ration; withdraw 5 days before slaughter; do not feed to layers; avoid contact with skin, eyes, or clothing; keep out of lakes, ponds, or streams.

(7) *Amount per ton.* Halofuginone 2.72 grams (0.0003 percent) plus lincomycin 2 to 4 grams.

(i) *Indications for use.* For the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima* and for improved feed efficiency.

(ii) *Limitations.* Feed continuously as sole ration; withdraw 4 days before slaughter; do not feed to layers; avoid contact with skin, eyes, or clothing; keep out of lakes, ponds, or streams.

[50 FR 33719, Aug. 21, 1985, as amended at 50 FR 42518, Oct. 21, 1985; 51 FR 7397, Mar. 3, 1986; 51 FR 11439, Apr. 3, 1986; 51 FR 14989, Apr. 22, 1986; 51 FR 23737, July 1, 1986; 53 FR 1018, Jan. 15, 1988; 53 FR 11065, Apr. 5, 1988; 54 FR 11519, Mar. 21, 1989]

§ 558.274 Hygromycin B.

(a) *Approvals.* (1) Type A medicated articles: 2.4 and 3 grams per pound to 000986 in § 510.600(c) of this chapter for use as in paragraph (c) of this section.

(2) 2.4 grams per pound to 011490, 016968, 018083, and 043733 in § 510.600(c) of this chapter for use in

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swine feed as in paragraph (c)(1)(ii) of this section.

(3) 1.2 grams per pound to 016968 in § 510.600(c) of this chapter for use in swine as in paragraph (c)(1)(ii) of this section.

(4) 0.6 gram per pound to 016968, 017519, 017790, 018083, 020275, 022422, 026948, 043733, 050568, and 050639 in § 510.600(c) of this chapter for use in chickens as in paragraph (c)(1)(i) of this section and in swine as in paragraph (c)(1)(ii) of this section.

(5) 0.48 and 2.4 grams per pound to 026186 in § 510.600(c) of this chapter for use in chickens as in paragraph (c)(1)(i) of this section and in swine as in paragraph (c)(1)(ii) of this section.

(6) 0.8 and 1.6 grams per pound to 043734 in § 510.600(c) of this chapter for use in chickens as in paragraph (c)(1)(i) of this section.

(7) 2.4 grams per pound to 011790 and 047427 in § 510.600(c) of this chapter for use in chickens as in paragraph (c)(1)(i) and in swine as in paragraph (c)(1)(ii) of this section.

(8) 0.6 and 1.6 grams per pound granted to 047863 in § 510.600(c) of this chapter for use in chickens as in paragraph (c)(1)(i) and in swine as in paragraph (c)(1)(ii) of this section.

(b) *Related tolerances.* See § 556.330 of this chapter.

(c) *Conditions of use.* (1) It may be used as follows:

Hygromycin B in grams per ton	Combination in grams per ton	Indications for use	Limitations	Spencer
(i) 8 to 12		Chickens: control of infestation of large roundworms (<i>Ascaris galli</i>), cecal worms (<i>Heterakis gallinae</i>), and capillary worms (<i>Capillaria obsignata</i>).	Withdraw 3 days before slaughter.	000888, 016968, 017519, 017790, 018083, 020275, 022422, 026948, 043733, 043734, 047427, 047863, 050568, 050639
	Bacitracin 100	Chickens: control of infestation of large roundworms (<i>Ascaris galli</i>), cecal worms (<i>Heterakis gallinae</i>), and capillary worms (<i>Capillaria obsignata</i>); treatment of chronic respiratory disease (airsac infection), blue comb (nonspecific infectious enteritis).	As bacitracin methylene disalicylate or zinc bacitracin; withdraw 3 days before slaughter.	
	Bacitracin plus penicillin (100 to 200 of combination).	1. Chickens: control of infestation of large roundworms (<i>Ascaris galli</i>), cecal worms (<i>Heterakis gallinae</i>), and capillary worms (<i>Capillaria obsignata</i>); treatment of chronic respiratory disease (airsac infection), blue comb (nonspecific infectious enteritis). 2. Chickens: control of infestation of large roundworms (<i>Ascaris galli</i>), cecal worms (<i>Heterakis gallinae</i>), and capillary worms (<i>Capillaria obsignata</i>); treatment of chronic respiratory disease (airsac infection), blue comb (nonspecific infectious enteritis).	Feed containing not less than 25% of penicillin plus not less than 50% of bacitracin; as procaine penicillin plus bacitracin methylene disalicylate; withdraw 3 days before slaughter. Combination containing not less than 50% nor more than 75% of bacitracin, except that it contains not more than 125 g of penicillin; as procaine penicillin plus zinc bacitracin; withdraw 3 days before slaughter.	

Hygromycin B in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
		3. Chickens, control of infestation of large roundworms (<i>Ascaris galli</i>), cecal worms (<i>Heterakis gallinae</i>), and capillary worms (<i>Capillaria obsignata</i>); treatment of chronic respiratory disease (airsac infection), blue comb (nonspecific infectious enteritis).	Combination containing 50% to 75% bacitracin, but not more than 125 g of penicillin, as procaine penicillin; withdraw 3 days before slaughter.	
	Chlortetracycline 100 to 200.	Chickens; control of infestation of large roundworms (<i>Ascaris galli</i>), cecal worms (<i>Heterakis gallinae</i>), and capillary worms (<i>Capillaria obsignata</i>); treatment of chronic respiratory disease (airsac infection), blue comb (nonspecific infectious enteritis); prevention of synovitis.	Not to be fed to laying chickens; as chlortetracycline hydrochloride; withdraw 3 days before slaughter.	
	Penicillin 100	Chickens; control of infestation of large roundworms (<i>Ascaris galli</i>), cecal worms (<i>Heterakis gallinae</i>), and capillary worms (<i>Capillaria obsignata</i>); treatment of chronic respiratory disease (airsac infection), blue comb (nonspecific infectious enteritis).	As procaine penicillin; withdraw 3 days before slaughter.	
	Penicillin plus streptomycin (90 to 180 of combination).	do	Feed containing 16.7% of penicillin; as procaine penicillin plus streptomycin sulfate; withdraw 3 days before slaughter.	
	Tylosin 4 to 50	Chickens: Control of infestations of large roundworms (<i>Ascaris galli</i>), cecal worms (<i>Heterakis gallinae</i>), and capillary worms (<i>Capillaria obsignata</i>); growth promotion and feed efficiency.	As tylosin phosphate; withdraw 3 days before slaughter.	000986
		Swine: control of infestation of large roundworms (<i>Ascaris suum</i>), nodular worms (<i>Oesophagostomum dentatum</i>), and whipworms (<i>Trichuris suis</i>).	Withdraw 15 days before slaughter.	000986, 011490, 016966, 017519, 017790, 018083, 020275, 022422, 026788, 026948, 043733, 047427, 047863, 050568, 050639
	Chlortetracycline 100 to 200.	Swine; control of infestation of large roundworms (<i>Ascaris suum</i>), nodular worms (<i>Oesophagostomum dentatum</i>) and whipworms (<i>Trichuris suis</i>); treatment of bacterial swine enteritis.	As chlortetracycline hydrochloride; withdraw 15 days before slaughter.	
	Tylosin 10 to 100	Swine: Control of infestations of large roundworms (<i>Ascaris suum</i>), nodular worms (<i>Oesophagostomum dentatum</i>), and whipworms (<i>Trichuris suis</i>); growth promotion and feed efficiency.	As tylosin phosphate; withdraw 15 days prior to slaughter; feed continuously as follows: Animal wt (lbs.): Up to 40.....20 to 100 ¹ 41 to 100.....20 to 40 ¹ 101 to market wt.....10 to 20 ¹	000986

¹Amount of Tylosin (g/t).

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(2) Hygromycin B may also be used in combination with:

- (i) Amprolium in accordance with § 558.55.
- (ii) Zoalene in accordance with § 558.680.

[41 FR 11000, Mar. 15, 1976]

EFFECTIVE DATE NOTE: At 54 FR 12596, Mar. 28, 1989, § 558.274 was amended by removing the number "017473" from paragraph (a)(4) and from the table of paragraph (c)(1) under the "Sponsor" column for entries (i) and (ii), effective April 7, 1989.

EDITORIAL NOTE: For FEDERAL REGISTER citations affecting § 558.274, see the List of CFR Sections Affected in the Finding Aids section of this volume.

§ 558.295 Iodinated casein.

(a) *Approvals.* See 017762 in § 510.600(c) of this chapter.

(b) *NAS/NRC status.* The use of this drug is NAS/NRC reviewed and found effective. Applications for these uses need not include efficacy data as required by § 514.111 of this chapter but may require bioequivalency or safety data.

(c) *Conditions of use—(1) Ducks—(i) Amount per ton.* 100 to 200 grams.

(ii) *Indications for use.* For increased rate of weight gain and improved feathering in growing ducks.

(2) *Dairy cows—(i) Amount per pound.* $\frac{1}{2}$ to 1½ grams per 100 lb of body weight.

(ii) *Indications for use.* For increased milk production in dairy cows.

(iii) *Limitations.* This drug is effective for limited periods of time, and the effectiveness is limited to the declining phase of lactation. Administration must be accompanied with increased feed intake; administration may increase heat sensitivity of the animal.

[45 FR 41631, June 20, 1980]

§ 558.311 Lasalocid.

(a) *Specifications.* A minimum of 90 percent of lasalocid activity is derived from lasalocid A.

(b) *Approvals.* Type A medicated articles approved for sponsors identified in § 510.600(c) of this chapter for use

as in paragraph (e) of this section follows:

(1) 3.0, 3.3, 3.8, 4.0, 4.3, 4.4, 5.0, 5.5, 5.7, 6.0, 6.3, 6.7, 7.2, 7.5, 8.0, 8.10.0, 12.5, 15, 20, and 50 percent activity to No. 000004 for use as in paragraphs (e)(1) (i), (ii), (iii), (iv), and (v) of this section.

(2) 15 percent activity to No. 000004 as provided by No. 000004 for use as in paragraph (e)(1)(v) of this section.

(3) 15, 20, 33.1, and 50 percent activity to No. 000004 for use in cattle feed as in paragraphs (e)(1)(vi), (vii), (ix), (xi), (xii), and (xiii) of this section, and for use in sheep as in paragraph (e)(1)(viii) of this section.

(4) 15 percent activity to No. 000004 for use in free-choice, mineral-vitamin Type C ruminant feeds as in paragraph (e)(2) of this section.

(5) 15 percent activity to 021930 (Type A article provided by 000004) for use in free-choice vitamin-mineral Type C cattle feeds as in paragraph (e)(1)(xi).

(c) *Related tolerance.* See § 556.347 of this chapter.

(d) *Special considerations.* (1) Type C cattle and sheep feeds may be manufactured from lasalocid liquid Type B feeds which have a pH of 4.0 to 8.0 and bear appropriate mixing directions as follows:

(i) For liquid Type B feeds stored in recirculating tank systems: Recirculate immediately prior to use for no less than 10 minutes, moving not less than 1 percent of the tank contents per minute from the bottom of the tank to the top. Recirculate daily as described even when not used.

(ii) For liquid Type B feeds stored in mechanical, air, or other agitation-type tank systems: Agitate immediately prior to use for not less than 10 minutes, creating a turbulence at the bottom of the tank that is visible at the top. Agitate daily as described even when not used.

(2) A positionally stable lasalocid liquid Type B feed will not be subject to the requirements for mixing directions prescribed in paragraph (d)(1) of this section provided it has a pH of 4.0 to 8.0 and contains a suspending agent(s) sufficient to maintain a vis-

costly of not less than 300 centipoises per second for 3 months. Form FDA 1900 must indicate the pH and centipoises per second for such lasalocid liquid Type B feed.

(3) If a manufacturer is unable to meet the requirements of paragraph (d)(1) or (2) of this section, the manufacturer may secure approval of a positionally stable liquid Type B feed by (i) either filing a new animal drug application for the product or establishing a master file containing data to support the stability of its product; (ii) authorizing the agency to reference and rely upon the data in the master file to support approval of a supplemental new animal drug application to establish positional stability; and (iii) requesting the sponsor of an approved new animal drug application to file a supplement to provide for use of its lasalocid Type A article in the manufacture of the liquid Type B feed specified in the appropriate master file. If the data demonstrate the stability of the liquid Type B feed described in the master file, the supplement new animal drug application will be approved. Approval of the supplement will not be published in the FEDERAL REGISTER because such approval will not affect or alter conditions or use of the product in the new animal drug application or the regulation. The approval will, however, provide a basis for the individual liquid feed manufacturer to submit, and for the agency to approve, a medicated feed application under section 512(m) of the act for liquid Type B feed. A manufacturer who seeks to market a positionally unstable lasalocid liquid Type B feed

with mixing directions different from the standard directions established in paragraph (d)(1) of this section may also follow this procedure.

(4) If adequate information is submitted to show that a particular liquid Type B feed containing lasalocid is stable outside the pH of 4.0 to 8.0, the pH restriction described in paragraphs (d)(1) and (2) of this section may be waived.

(5) Required label statements:

(i) For liquid Type B feed (cattle and sheep): Mix thoroughly with grain and/or roughage prior to feeding. Feeding undiluted, mixing errors, or inadequate mixing (recirculation or agitation) may result in an excess lasalocid concentration which could be fatal to cattle and sheep. Do not allow horses or other equines access to Type A articles or Type B feeds containing lasalocid as ingestion may be fatal. Safety of lasalocid for use in unapproved species has not been established.

(ii) For Type A articles or Type B feeds (cattle and sheep): Feeding undiluted or mixing errors may result in an excess lasalocid concentration which could be fatal to cattle and sheep. Do not allow horses or other equines access to Type A articles or Type B feeds containing lasalocid as ingestion may be fatal. Safety of lasalocid for use in unapproved species has not been established.

(6) Lasalocid Type A medicated articles containing lasalocid dried fermentation residue are for use in cattle and sheep feed only.

(e)(1) *Conditions of use.* It is used as follows:

Lasalocid sodium activity in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
9.98 (0.0075 pct) to 113 (0.0125 pct).		For the prevention of coccidiosis caused by <i>Eimeria tenella</i> , <i>E. necatrix</i> , <i>E. acervulina</i> , <i>E. brunetti</i> , <i>E. mivati</i> , and <i>E. maxima</i> .	For broiler or fryer chickens only; feed continuously as the sole ration.	000004
9.98 (0.0075 pct) to 113 (0.0125 pct).	Roxarsone 45.4 (0.005 pct).	Broiler or fryer chickens; for the prevention of coccidiosis caused by <i>Eimeria tenella</i> , <i>E. necatrix</i> , <i>E. acervulina</i> , <i>E. brunetti</i> , <i>E. mivati</i> , and <i>E. maxima</i> and as an aid in the reduction of lesions due to <i>E. tenella</i> .	For broiler or fryer chickens only; feed continuously as the sole ration; as sole source of organic arsenic; withdraw 5 d before slaughter; roxarsone provided by Nos. 017210 and 011801 in § 510.600(c) of this chapter.	000004

Lasalocid sodium activity in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
	Roxarsone 45.4 plus bambermycins 1 (0.00011 pct).	For prevention of coccidiosis caused by <i>Eimeria tenella</i> , <i>E. necatrix</i> , <i>E. acervulina</i> , <i>E. brunetti</i> , <i>E. mivati</i> , and <i>E. maxima</i> ; as an aid in the reduction of lesions due to <i>E. tenella</i> ; and for increased rate of weight gain.	For broiler chickens only; feed continuously as sole ration; withdraw 5 days before slaughter; roxarsone provided by Nos. 017210 and 011801 in § 510.600(c) of this chapter, bambermycins provided by No. 012799.	000004
	Roxarsone 45.4 plus lincomycin 2.0.	For prevention of coccidiosis caused by <i>Eimeria tenella</i> , <i>E. necatrix</i> , <i>E. acervulina</i> , <i>E. brunetti</i> , <i>E. mivati</i> , and <i>E. maxima</i> ; as an aid in the reduction of lesions due to <i>E. tenella</i> ; and for increased rate of weight gain and improved feed efficiency.	For broiler chickens only; feed continuously as sole ration; withdraw 5 days before slaughter; roxarsone provided by Nos. 017210 and 011801 in § 510.600(c) of this chapter, lincomycin provided by No. 000009.	000004
	Roxarsone 45.4 plus bacitracin 10 to 25.	For prevention of coccidiosis caused by <i>Eimeria tenella</i> , <i>E. necatrix</i> , <i>E. acervulina</i> , <i>E. brunetti</i> , <i>E. mivati</i> , and <i>E. maxima</i> ; as an aid in the reduction of lesions due to <i>E. tenella</i> ; and for increased rate of weight gain.	For broiler or fryer chickens only; feed continuously as the sole ration; withdraw 5 days before slaughter; roxarsone provided by Nos. 017210 and 011801 in § 510.600(c) of this chapter, bacitracin methylene disalicylate provided by No. 046573 in § 510.600(c) of this chapter.	000004
	Roxarsone 45.4 plus bacitracin 10 or 30.	For prevention of coccidiosis caused by <i>E. tenella</i> , <i>E. necatrix</i> , <i>E. acervulina</i> , <i>E. brunetti</i> , <i>E. mivati</i> and <i>E. maxima</i> ; as an aid in the reduction of lesions due to <i>E. tenella</i> ; and for increased rate of weight gain (10 grams per ton) or improved feed efficiency (30 grams per ton).	For broiler chickens only; feed continuously as sole ration; withdraw 5 days before slaughter; roxarsone provided by Nos. 017210 and 011801 in § 510.600(c) of this chapter, bacitracin zinc provided by No. 011716.	000004
	Roxarsone 45.5 plus bacitracin methylene disalicylate 50.	Prevention of coccidiosis caused by <i>Eimeria necatrix</i> , <i>E. tenella</i> , <i>E. acervulina</i> , <i>E. brunetti</i> , <i>E. mivati</i> , and <i>E. maxima</i> ; reduction of lesions due to <i>E. tenella</i> ; prevention of necrotic enteritis caused or complicated by <i>Clostridium</i> spp. or other susceptible organisms.	Feed continuously as sole ration; as sole source of organic arsenic; withdraw 5 days before slaughter.	046573
(iii) 66 (0.0075 pct).....	Lincomycin 2 (0.00022 pct).	Broiler or fryer chickens; for the prevention of coccidiosis caused by <i>Eimeria mivati</i> , <i>E. brunetti</i> , <i>E. tenella</i> , <i>E. acervulina</i> , <i>E. maxima</i> , and <i>E. necatrix</i> ; for increased rate of weight gain and improved feed efficiency.	For broiler and fryer chickens only; feed continuously as sole ration; withdraw 5 d before slaughter; Type C feed must be used within 4 weeks of manufacture; as lincomycin hydrochloride monohydrate.	000004
(iv) 66 (0.0075 percent).	Bacitracin 10 to 50.....	For prevention of coccidiosis caused by <i>Eimeria tenella</i> , <i>E. necatrix</i> , <i>E. acervulina</i> , <i>E. brunetti</i> , <i>E. mivati</i> , and <i>E. maxima</i> , and for increased rate of weight gain and improved feed efficiency.	For broiler or fryer chickens only; feed continuously as the sole ration; withdraw 3 days before slaughter bacitracin methylene disalicylate provided by No. 046573 in § 510.600(c) of this chapter.	000004
(v) 66 (0.0075 pct) to 113 (0.0125 pct).	Virginiamycin 20.....	For prevention of coccidiosis caused by <i>Eimeria tenella</i> , <i>E. necatrix</i> , <i>E. acervulina</i> , <i>E. brunetti</i> , <i>E. mivati</i> , and <i>E. maxima</i> , and for increased rate of weight gain and improved feed efficiency.	For broiler and fryer chickens only; feed continuously as sole ration; do not feed to laying chickens; lasalocid sodium provided by No. 000004 in § 510.600(c) of this chapter.	000007

Lasalocid sodium activity in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
10 (0.0011 pct) to 30 (0.0033 pct)		Cattle; for improved feed efficiency.	In Type C feeds; for cattle fed in confinement for slaughter only; feed continuously in complete feed to provide not less than 100 mg nor more than 360 mg of lasalocid sodium activity per head per day.	000004
	Oxytetracycline 7.5	Cattle; for improved feed efficiency and reduction of incidence and severity of liver abscesses.	In Type C feeds, for beef cattle fed in confinement for slaughter; feed continuously at 100 to 360 mg/head/day lasalocid and 75 mg/head/day oxytetracycline. As monoalkyl (C ₈ -C ₁₂) trimethyl ammonium oxytetracycline.	000004
25 (0.0027 pct) to 30 (0.0033 pct)		Cattle; for improved feed efficiency and increased rate of weight gain.	In Type C feeds; for cattle fed in confinement for slaughter only; feed continuously in complete feed to provide not less than 250 mg nor more than 360 mg of lasalocid sodium activity per head per day.	000004
	Oxytetracycline 7.5	Cattle; for improved feed efficiency, increased rate of weight gain, and reduction of incidence and severity of liver abscesses.	In Type C feeds, for beef cattle fed in confinement for slaughter; feed continuously at 250 to 360 mg/head/day lasalocid and 75 mg/head/day oxytetracycline. As monoalkyl (C ₈ -C ₁₂) trimethyl ammonium oxytetracycline.	000004
20 (0.0022 pct) to 30 (0.0033 pct)		Sheep; for the prevention of coccidiosis caused by <i>Eimeria ovina</i> , <i>E. crandallis</i> , <i>E. ovinoidalis</i> (<i>E. ninakohlyaki-movae</i>), <i>E. parva</i> , and <i>E. intricata</i> .	In Type C feeds; for sheep maintained in confinement; feed continuously in complete feed to provide not less than 15 mg nor more than 70 mg of lasalocid sodium activity per head per day depending on body weight.	000004
		Cattle; for increased rate of weight gain.	For pasture cattle (slaughter, stocker, feeder cattle, and dairy and beef replacement heifers) only; feed continuously at a rate of not less than 60 mg nor more than 200 mg of lasalocid per head per day; when on pasture; the drug must be contained in at least 1 pound of feed.	000004
8 (0.0075 pct) to 13 (0.0125 pct)	Bacitracin 4 to 50	Broiler chickens; for prevention of coccidiosis caused by <i>Eimeria tenella</i> , <i>E. necatrix</i> , <i>E. acervulina</i> , <i>E. brunetti</i> , <i>E. mivati</i> , and <i>E. maxima</i> ; and for improved feed efficiency.	For broiler chickens only; feed continuously as the sole ration; withdraw 3 days before slaughter; bacitracin methylene disalicylate provided by No. 046573 in § 510.600(c) of this chapter.	000004

Lasalocid sodium activity in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
(xi).....		Cattle; for increased rate of weight gain.	For pasture cattle (slaughter, stocker, feeder cattle, and dairy and beef replacement heifers) only; feed continuously on a free-choice basis at a rate of not less than 60 mg nor more than 200 mg of lasalocid per head per day. Each use in a free-choice Type C feed must be the subject of an approved NADA or supplemental NADA as provided in § 510.455 of this chapter.	000004 021800
(xii) 10 (0.0011 pct) to 30 (0.0033 pct).	Melengestrol acetate 0.25 to 2.	Heifers; for increased rate of weight gain, improved feed efficiency, and suppression of estrus (heat).	In Type C feeds; heifers fed in confinement for slaughter only; feed continuously in Type C feed to provide not less than 100 mg nor more than 360 mg of lasalocid sodium activity per head per day and 0.25 mg to 0.5 mg of melengestrol acetate per head per day; withdraw melengestrol acetate 48 hours prior to slaughter; lasalocid sodium provided by No. 000004 in § 510.600(c) of this chapter; melengestrol acetate provided by No. 000009 in § 510.600(c) of this chapter and used as in § 558.342(c)(3).	
(xiii).....		Cattle; for control of coccidiosis caused by <i>Eimeria bovis</i> and <i>Eimeria zuernii</i> .	For cattle; feed continuously at a rate of 1 mg of lasalocid per 2.2 pounds body weight per day to cattle weighing up to 800 pounds with a maximum of 360 mg of lasalocid per head per day.	000004

(2) It is used as a free-choice mineral Type C feed as follows:

(i) Specifications.

Ingredient	Per- cent	Interna- tional feed No.
Defluorinated Phosphate (20.5 percent Calcium, 18.5 percent Phosphorus).....	35.9	6-01-080
Sodium Chloride (Salt).....	20.0	6-04-152
Calcium Carbonate (38 percent Calcium).....	18.0	6-01-069
Cottonseed Meal.....	10.0	5-01-621
Potassium Chloride.....	3.0	6-03-755
Selenium Premix (0.02 percent Selenium) ¹	3.0	
Dried Cane Molasses.....	2.5	4-04-695
Magnesium Sulfate.....	1.7	6-02-758
Vitamin Premix ¹	1.4	
Magnesium Oxide.....	1.2	6-02-756
Potassium Sulfate.....	1.2	6-06-098
Trace Mineral Premix ¹	1.04	
Bovatec Premix (68 grams per pound).....	1.06	

¹ Content of the vitamin and trace mineral premixes may be varied; however, they should be comparable to those

used by the firm for other free-choice feeds. Formulation modifications require FDA approval prior to marketing. The amount of selenium and ethylenediamine dihydroiodide (EDDI) must comply with published regulations. For selenium (21 CFR 573.920): up to 120 parts per million in a medium for free-choice feeding at a rate not to exceed an intake of 3 milligrams per head per day. For EDDI (51 FR 11483; April 2, 1986): 10 milligrams per head per day.

(ii) Amount. 1,440 grams per ton (0.16 percent).

(iii) Indications for use. Cattle, for increased rate of weight gain.

(iv) Limitations. For pasture cattle (slaughter, stocker, feeder cattle, and dairy and beef replacement heifers); feed continuously on a free-choice basis at a rate of 60 to 200 milligrams lasalocid per head per day; each use of this Type C free-choice feed must be the subject of an approved FD-1900 as provided in § 510.455 of this chapter.

(v) Sponsor. See No. 000004 in § 510.600(c) of this chapter.

(41 FR 44382, Oct. 8, 1976)

EDITORIAL NOTE: For FEDERAL REGISTER citations affecting § 558.311, see the List of CFR Sections Affected in the Finding Aids section of this volume.

§ 558.315 Levamisole hydrochloride (equivalent).

(a) *Approvals.* Type A medicated articles: 227 grams per pound to 043781 in § 510.600(c) of this chapter.

(b) *Related tolerances.* See § 556.350 of this chapter.

(c) *Conditions of use.* It is used in Type C medicated feed as follows:

(1) *Cattle—(i) Amount per pound.* 0.36–3.6 grams (0.08–0.8 percent).

(ii) *Indications for use.* Treatment of the following gastrointestinal worms and lung worm infections; stomach worms (*Haemonchus*, *Trichostrongylus*, *Ostertagia*), intestinal worms (*Trichostrongylus Cooperia*, *Nematodirus*, *Benostomum*, *Oesophagostomum*), and lungworms (*Dictyocaulus*).

(iii) *Limitations.* Administer medicated feed mixed thoroughly in one half the usual amount of morning feed; the medicated feed mix should be consumed within 6 hours; when medicated feed is consumed resume normal feeding; medicated feed is to be fed at the rate of 0.36 gram of levamisole hydrochloride (equivalent) per 100 lb. of body weight; conditions of constant helminth exposure may require retreatment within 2 to 4 weeks after the first treatment; do not slaughter for food within 48 hours of treatment; consult veterinarian before using in severely debilitated animals; do not administer to dairy animals of breeding age; for use in pelleted or meal feeds only; the label shall bear the caution, "Muzzle foam may be observed. However, this reaction will disappear within a few hours. If this condition persists, a veterinarian should be consulted. Follow recommended dosage carefully."

(2) *Swine—(i) Amount per pound.* 36 grams (0.08 percent).

(ii) *Indications for use.* Treatment of the following nematode infections: large roundworms (*Ascaris suum*), nodular worms (*Oesophagostomum* sp.), lungworms (*Metastrongylus* sp.), intestinal threadworms (*Strongylus edentatus*), swine kidney worms (*Stephanurus dentatus*).

(iii) *Limitations.* It is recommended that regular feed be withheld overnight and worming feed administered the following morning; dilute supplement with nonmedicated feed as directed; feed the equivalent of 1 lb. of 0.08 percent worming feed per 100 lbs. of body weight of pigs to be treated; may be fed as sole feed or thoroughly mixed with 1 to 2 parts of regular feed prior to feeding; when medicated feed is consumed, resume normal feeding. Pigs maintained under conditions of constant worm exposure may require retreatment within 4 to 5 weeks after the first treatment due to reinfection; do not slaughter for food within 72 hours of treatment; the label shall bear the caution, "Excessive salivation or muzzle foam may be observed. This reaction is occasionally seen and will disappear in a short time after medication. If pigs are infected with mature lungworms, coughing and vomiting may be observed soon after medicated feed is consumed. This reaction is due to the expulsion of worms from the lungs and will be over in several hours."

[40 FR 13959, Mar. 27, 1975, as amended at 43 FR 11176, Mar. 17, 1978; 43 FR 39351, Sept. 5, 1978; 43 FR 16013, Mar. 16, 1979; 51 FR 7398, Mar. 3, 1986]

§ 558.325 Lincomycin.

(a) *Approvals.* Type A articles and Type B feeds approved for sponsors in § 510.600(c) of this chapter for specific uses as in paragraph (c) of this section as follows:

(1) No. 000009: (i) 4 grams per pound as in paragraphs (c) (1) and (3) of this section.

(ii) 20 grams per pound as in paragraphs (c) (1) through (3) of this section.

(iii) 50 grams per pound as in paragraphs (c) (1) and (2) of this section.

(iv) 10 grams per pound as in paragraphs (c)(1) and (2) (i) through (iv) of this section.

(2) No. 034139 for 4 grams per pound as in paragraphs (c)(2) (i) through (iv) of this section.

- (3) [Reserved]
- (4) No. 011490 for 8, 10, and 20 grams per pound as in paragraphs (c)(2) (i) through (iii) of this section.
- (5) Nos. 043733, 050639, and 051359 for 8 and 20 grams per pound as in paragraphs (c)(2) (i) through (iii) of this section.
- (6) No. 018083 for 4, 8, 10, and 20 grams per pound as in paragraphs (c)(2) (i) through (iii) of this section.
- (7) [Reserved]
- (8) No. 016968 for 4, 5, 8, 10, and 20 grams per pound as in paragraphs (c)(2) (i) through (iii) of this section.
- (9) No. 047427 for 4 and 20 grams per pound as in paragraphs (c)(2) (i) through (iv) of this section.
- (10) No. 017274 for 4, 8, and 20 grams per pound as in paragraphs (c)(2) (i) through (iii) of this section.
- (11) No. 012286 for 5 and 10 grams per pound as in paragraphs (c)(2) (i) through (iii) of this section.
- (12) No. 020275 for 20 grams per pound as in paragraphs (c)(2) (i) through (iii) of this section.
- (13) No. 017800 for 2.5 and 8 grams per pound as in paragraphs (c)(2) (i) through (iv) of this section.
- (14) No. 024174 for 4 and 20 grams per pound as in paragraphs (c)(2) (i) through (iii) of this section.
- (15) No. 017790 for 8 and 20 grams per pound as in paragraphs (c)(2) (i) through (iv) of this section.
- (b) *Related tolerances in edible products.* See § 556.360 of this chapter.
- (c) *Conditions of use—(1) Broilers:*
 - (i) *Amount per ton.* 2 to 4 grams.
 - (a) *Indications for use.* For increase in rate of weight gain and improved feed efficiency.
 - (b) *Limitations.* As lincomycin hydrochloride monohydrate.
 - (ii) *Amount per ton.* 2 grams.
 - (a) *Indications for use.* For control of necrotic enteritis caused by *Clostridium* spp. or other susceptible organisms.
 - (b) *Limitations.* As lincomycin hydrochloride monohydrate.
- (2) *Swine—(i) Amount per ton.* 40 grams.
- (a) *Indications for use.* For control of swine dysentery.
- (b) *Limitations.* Feed as sole ration; for use in swine on premises with a history of swine dysentery but where

symptoms have not yet occurred; not to be fed to swine that weigh more than 250 pounds; withdraw 6 days before slaughter.

(ii) *Amount per ton.* 100 grams; 40 grams.

(a) *Indications for use.* For treatment and control of swine dysentery.

(b) *Limitations.* Feed 100 grams per ton for 3 weeks or until signs of disease disappear, followed by 40 grams per ton; feed as sole ration; not to be fed to swine that weigh more than 250 pounds; withdraw 6 days before slaughter.

(iii) *Amount per ton.* 100 grams.

(a) *Indications for use.* For treatment of swine dysentery.

(b) *Limitations.* Feed as sole ration for 3 weeks or until signs of disease disappear; not to be fed to swine that weigh more than 250 pounds; withdraw 6 days before slaughter.

(iv) *Amount per ton.* 200 grams.

(a) *Indications for use.* For reduction in the severity of swine mycoplasma pneumoniae caused by *Mycoplasma hyopneumoniae*.

(b) *Limitations.* Feed as sole ration for 21 days; not to be fed to swine that weigh more than 250 pounds; withdraw 6 days before slaughter.

(v) *Amount per ton.* 20 grams.

(a) *Indications for use.* For increased rate of weight gain in growing-finishing swine.

(b) *Limitations.* Feed as sole ration; not for use in swine weighing over 250 pounds; withdraw 6 days before slaughter.

(3) Lincomycin may also be used for broilers in combination with:

(i) Amprolium, ethopabate, and roxarsone in accordance with §§ 558.58 and 558.530.

(ii) Amprolium and ethopabate in accordance with § 558.58.

(iii) Clopidol in accordance with § 558.175.

(iv) Buquinolate in accordance with § 558.105.

(v) Decoquinolate in accordance with § 558.195.

(vi) Zoalene in accordance with § 558.680.

(vii) Monensin in accordance with § 558.355.

(viii) Robenidine hydrochloride in accordance with § 558.515.

(ix) Roxarsone, monensin sodium in accordance with §§ 558.355 and 558.530.

(x) Lasalocid sodium in accordance with § 558.311.

(xi) Nicarbazine and roxarsone as in § 558.366.

(xii) Nicarbazine as in § 558.366.

(xiii) Lasalocid sodium and roxarsone as in § 558.311.

(xiv) Halofuginone in accordance with § 558.265.

(4) Lincomycin may also be used for swine in combination with:

(i) Pyrantel tartrate as in § 558.485.

(ii) [Reserved]

[40 FR 13959, Mar. 27, 1975]

EDITORIAL NOTE: For FEDERAL REGISTER citations affecting § 558.325, see the List of CFR Sections Affected in the Finding Aids section of this volume.

§ 558.340 Maduramicin ammonium.

(a) *Approvals.* Type A medicated articles: 4.54 grams per pound to 010042 in § 510.600(c) of this chapter.

(b) *Tolerances.* See § 556.375 of this chapter.

(c) *Conditions of use.* (1) *Amount.* 4.54 to 5.45 grams per ton (5 to 6 parts per million) (1 to 1.2 pounds per ton).

(2) *Indications for use.* For prevention of coccidiosis caused by *Eimeria acervulina*, *E. tenella*, *E. brunetti*, *E. maxima*, *E. necatrix*, and *E. mivati*.

(3) *Limitations.* For broiler chickens only. Feed continuously as sole ration. Do not feed to laying hens. Withdraw 5 days before slaughter.

[54 FR 5229, Feb. 2, 1989]

§ 558.342 Melengestrol acetate.

(a) *Approvals.* Dry Type A medicated articles: 100 or 200 milligrams per pound or liquid Type A article containing 500 milligrams per pound to 000009 in § 510.600(c) of this chapter.

(b) *Related tolerances.* See § 556.380 of this chapter.

(c) *Conditions of use.* It is used for heifers as follows:

(1) *Amount.* Melengestrol acetate, 0.25 to 0.50 milligram per head per day.

(i) *Indications for use.* For increased rate of weight gain, improved feed efficiency, and suppression of estrus (heat).

(ii) *Limitations.* Heifers being fed for slaughter; administer in Type B feed; withdraw 48 hours prior to slaughter.

(2) *Amount.* Melengestrol acetate, 0.25 to 1.6 grams per ton (to provide 0.25 to 0.40 milligram per head per day), plus monensin, 5 to 30 grams per ton (to provide 50 to 360 milligrams per head per day), see § 558.335(f)(3)(iv).

(i) *Indications for use.* For increased rate of weight gain, improved feed efficiency, and suppression of estrus (heat).

(ii) *Limitations.* Heifers being fed in confinement for slaughter: Administer melengestrol acetate and monensin by (a) adding melengestrol acetate from a separate Type B feed containing 0.125 to 0.8 milligram per pound to Type C medicated feeds containing monensin at 5 to 30 grams per ton, (b) adding melengestrol acetate from a separate Type B feed containing 0.125 to 0.8 milligram per pound and monensin from a separate Type B feed containing 50 to 1,200 grams per ton to Type C medicated feeds, (c) adding melengestrol acetate and monensin which are contained in the same dry Type B feed at the ranges in paragraphs (c)(2)(ii) (a) and (b) of this section to Type C medicated feeds, or (d) using a liquid Type B feed containing 0.125 to 0.8 milligram melengestrol acetate per pound and 25 to 600 milligrams monensin per pound (50 to 1,200 grams per ton) to make Type C medicated feeds. Type C medicated feeds in paragraphs (c)(2)(ii) (a) and (b) of this section may be manufactured from monensin liquid Type B feeds in accordance with paragraph (f)(3)(i)(b) of § 558.355. Withdraw melengestrol acetate 48 hours prior to slaughter.

(3) *Amount.* Melengestrol acetate, 0.25 to 2.0 grams per ton (to provide 0.25 to 0.50 milligram per head per day), plus lasalocid sodium, 10 to 30 grams per ton (to provide 100 to 360 milligrams per head per day), see § 558.311(e)(1)(xii).

(i) *Indications for use.* For increased rate of weight gain, improved feed efficiency, and suppression of estrus (heat).

(ii) *Limitations.* Heifers being fed in confinement for slaughter. Withdraw

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melengestrol acetate 48 hours prior to slaughter. Lasalocid sodium as provided by No. 000004 in § 510.600(c) of this chapter.

[42 FR 28535, June 3, 1977, as amended at 46 FR 18967, Mar. 27, 1981; 49 FR 39842, Oct. 11, 1984; 50 FR 1843, Jan. 14, 1985; 50 FR 16226, Apr. 25, 1985; 51 FR 7398, Mar. 3, 1986; 51 FR 36222, Oct. 9, 1986; 52 FR 2685, Jan. 26, 1987; 52 FR 33804, Sept. 8, 1987; 53 FR 27959, July 26, 1988]

§ 558.348 Mibolerone.

(a) *Approvals.* To No. 000009 in § 510.600(c) of this chapter for a canned dog food, each 6½ ounce can containing 30 or 60 micrograms of mibolerone.

(b) *Conditions of use—(1) Amount.* 30 micrograms for animals weighing up to 25 pounds; 60 micrograms for animals weighing 26 to 50 pounds; 120 micrograms for animals weighing 51 to 100 pounds; 180 micrograms for animals weighing over 100 pounds, or German Shepherds or German Shepherd mix weighing 30 to 80 pounds.

(2) *Indications for use.* For the prevention of estrus (heat) in adult female dogs not intended primarily for breeding purposes.

(3) *Limitations.* Administer daily at least 30 days before expected initiation of heat and continue as long as desired, but for not more than 12 months. Mibolerone should not be used in bitches before first estrous period or in purebred Bedlington terriers. It is not intended for animals being used primarily for breeding purposes. Use orally in adult female dogs only. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[47 FR 6617, Feb. 16, 1982]

§ 558.355 Monensin.

(a) *Specifications.* Monensin is present as monensin or the sodium salt. A minimum of 90 percent of monensin activity is derived from monensin A.

(b) *Approvals.* Approvals for Type A medicated articles containing the specified levels of monensin activity granted to firms identified by sponsor numbers in § 510.890(c) of this chapter for

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the conditions of use indicated in paragraph (f) of this section are as follows:

(1) To 000986: 36.3 (for export only), 44, 45, or 60 grams per pound, paragraphs (f)(1)(i) and (4) of this section.

(2) To 000986: 110 grams per lb., paragraphs (f)(1) (i), (iii), (iv), (v), (ix), and (x).

(3) To 000986: 44 grams per lb. with 18 grams per lb. of roxarsone, 110 grams per lb. with 45 grams per lb. of roxarsone, paragraph (f)(1)(ii).

(4) To 000986: 45 grams per pound, as monensin sodium, paragraph (f)(2) of this section.

(5) To 000007: 45 grams per pound, as monensin sodium provided by No. 000986, paragraphs (f)(1) (xiii), (xx), and (xxi) of this section.

(6) To 000986: 45 grams per pound, as monensin sodium, paragraph (f)(5) of this section.

(7) To 000986: 20, 30, 45, or 60 grams per pound, as monensin sodium, paragraph (f)(3) of this section.

(8) To 010042: 45 grams per pound, as monensin sodium provided by No. 000986, paragraph (f)(1)(xiv) of this section.

(9) To 011716: 45 grams per pound, as monensin sodium provided by No. 000986, paragraphs (f)(1) (xv), (xvi), and (xvii) of this section.

(10) [Reserved]

(11) To 046573: paragraph (f)(1) (xviii), (xix), (xxiii), and (xxiv) of this section.

(12) To 000069: paragraph (f)(1)(xxii) of this section.

(13) To 021930: 60 grams per pound, paragraph (f)(3)(v) of this section.

(c) *Assay limits.* Liquid Type B feeds contain 80 to 120 percent of the labeled amount of monensin activity.

(d) *Special considerations.* (1) Type C chicken feed containing monensin as the mycelial cake shall bear an expiration date of 90 days after its date of manufacture.

(2) Type C cattle feeds containing 30 grams or less monensin sodium per ton shall bear an expiration date of 30 days after its date of manufacture.

(3) [Reserved]

(4) [Reserved]

(5) Liquid Type B feeds shall bear an expiration date of 8 weeks after its date of manufacture.

(6) The labeling of all formulations containing monensin shall bear the following caution statement: Do not allow horses or other equines access to formulations containing monensin. Ingestion of monensin by equines has been fatal.

(7) The labeling of all Type A articles and Type B feeds (liquid and dry) containing monensin intended for use in cattle shall bear, in addition to the caution statement in paragraph (d)(6) of this section, the following caution statements:

(i) Monensin medicated cattle feed is safe for use in cattle only. Consumption by unapproved species may result in toxic reactions;

(ii) Feeding undiluted or mixing errors resulting in high concentrations of monensin could be fatal to cattle;

(iii) Must be thoroughly mixed in feeds before use;

(iv) Do not feed undiluted;

(v) Do not exceed the levels of monensin recommended in the feeding directions, as reduced average daily gains may result.

(8) The labeling of complete feeds containing monensin intended for use in cattle shall bear the caution statements specified in paragraphs (d) (6) and (7) (i) and (v) of this section.

(9) The labeling of Type A articles containing monensin intended for use in chickens shall bear the caution statements specified in paragraphs (d) (6) and (7) (iii) and (iv) of this section.

(e) *Related tolerances.* See § 556.420 of this chapter.

(f) *Conditions of use.* It is used as follows:

(1) *Broiler chickens—(i) Amount per ton.* Monensin, 90-110 grams.

(a) *Indications for use.* As an aid in the prevention of coccidiosis caused by *E. necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*.

(b) *Limitations.* Do not feed to laying chickens; feed continuously as the sole ration; in the absence of coccidiosis, the use of monensin with no withdrawal period may limit feed intake resulting in reduced weight gain; as monensin or monensin sodium.

(ii) *Amount per ton.* Monensin, 90-110 grams, plus roxarsone 45.4 grams (0.05 percent).

(a) *Indications for use.* Growth promotion and feed efficiency, improving pigmentation; as an aid in the prevention of coccidiosis caused by *E. necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati* and *E. maxima*.

(b) *Limitations.* Do not feed to laying chickens; feed continuously as the sole ration; withdraw 5 days before slaughter; as sole source of organic arsenic; as monensin or monensin sodium.

(iii) *Amount per ton.* Monensin, 90-110 grams plus bacitracin, 5-25 grams.

(a) *Indications for use.* For increased rate of weight gain and improved feed efficiency; as an aid in the prevention of coccidiosis caused by *E. necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*.

(b) *Limitations.* Do not feed to laying chickens; feed continuously as sole ration; in the absence of coccidiosis, the use of monensin with no withdrawal period may limit feed intake resulting in reduced weight gain; as bacitracin methylene disalicylate provided by No. 046573 in § 510.600(c) of this chapter; as monensin sodium.

(iv) *Amount per ton.* Monensin, 90-110 grams plus bacitracin, 10 grams.

(a) *Indications for use.* For increased rate of weight gain and improved feed efficiency; as an aid in the prevention of coccidiosis caused by *E. necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*.

(b) *Limitations.* Do not feed to laying chickens; feed continuously as sole ration; in the absence of coccidiosis, the use of monensin with no withdrawal period may limit feed intake resulting in reduced weight gain; as zinc bacitracin provided by No. 011716 in § 510.600(c) of this chapter; as monensin sodium.

(v) *Amount per ton.* Monensin, 90-110 grams plus bacitracin, 10-30 grams.

(a) *Indications for use.* For improved feed efficiency; as an aid in the prevention of coccidiosis caused by *E. necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*.

(b) *Limitations.* Do not feed to laying chickens; feed continuously as sole ration; in the absence of coccidiosis, the use of monensin with no withdrawal period may limit feed intake

resulting in reduced weight gain; as zinc bacitracin provided by No. 011716 in § 510.600(c) of this chapter; as monensin sodium.

(vi) *Amount per ton.* Monensin, 90 to 110 grams plus bambermycins, 1 to 2 grams. See § 558.95(b)(1)(vi).

(vii) *Amount per ton.* Monensin, 90 to 110 grams plus bambermycins, 1 gram plus roxarsone, 22.7 to 45.4 grams (.0025 to .005 percent). See § 558.95(b)(1)(vii).

(viii) *Amount per ton.* Monensin, 90 to 110 grams plus oxytetracycline, 200 grams.

(a) *Indications for use.* As an aid in the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*; and for the control of complicated chronic respiratory disease (CRD or air-sac infection) caused by *Mycoplasma gallisepticum* and *Escherichia coli*.

(b) *Limitations.* In the absence of coccidiosis, the use of monensin with no withdrawal period may limit feed intake resulting in reduced weight gain; do not feed to laying chickens; feed continuously as sole ration; as monensin sodium.

(ix) *Amount per ton.* Monensin, 90-110 grams plus lincomycin, 2 grams.

(a) *Indications for use.* For increase in rate of weight gain and improved feed efficiency; as an aid in the prevention of coccidiosis caused by *E. necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*.

(b) *Limitations.* Do not feed to laying chickens; to be fed as a sole ration; in the absence of coccidiosis, the use of monensin with no withdrawal period may limit feed intake resulting in reduced weight gain; as monensin sodium.

(x) *Amount per ton.* Monensin, 90-110 grams plus lincomycin, 2 grams and roxarsone, 15-45 grams.

(a) *Indications for use.* For increase in rate of weight gain; as an aid in the prevention of coccidiosis caused by *E. necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*.

(b) *Limitations.* Do not feed to laying chickens; feed continuously as the sole ration; withdraw 5 days before slaughter; as sole source of organic arsenic; as roxarsone provided by No.

017210, § 510.600(c) of this chapter; monensin sodium provided by 000986, § 510.600(c) of this chapter; lincomycin provided by No. 000986, § 510.600(c) of this chapter; as a combination provided by No. 000986, § 510.600(c) of this chapter.

(xi) *Amount per ton.* Monensin, 110 grams, plus lincomycin, 2 grams and roxarsone, 15 to 30 grams.

(a) *Indications for use.* For increase in rate of weight gain, improved efficiency, improved pigmentation and as an aid in the prevention of coccidiosis caused by *E. necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati* and *E. maxima*.

(b) *Limitations.* Do not feed to laying chickens; feed continuously as the sole ration; withdraw 5 days before slaughter; as sole source of organic arsenic; as roxarsone provided by 017210 in § 510.600(c) of this chapter; as monensin sodium provided by 000986 in § 510.600(c) of this chapter; as lincomycin provided by No. 000986 in § 510.600(c) of this chapter; as a combination provided by No. 000986, § 510.600(c) of this chapter.

(xii) *Amount per ton.* Monensin, 110 to 110 grams, plus bacitracin methylene disalicylate, 10 to 25 grams, and roxarsone, 11.3 to 45.4 grams.

(a) *Indications for use.* As an aid in the prevention of coccidiosis caused by *E. necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. maxima*, and *E. mivati*; for increased rate of weight gain and for improved feed efficiency.

(b) *Limitations.* Do not feed to laying chickens; feed continuously as sole ration; withdraw 5 days before slaughter; as sole source of organic arsenic; as monensin sodium provided by No. 000986 in § 510.600 of this chapter; as bacitracin methylene disalicylate provided by No. 048573 in § 510.600 of this chapter; as roxarsone provided by No. 011801 or 017210 in § 510.600 of this chapter.

(xiii) *Amount per ton.* Monensin, 90 to 110 grams, plus 5 grams virginiamycin.

(a) *Indications for use.* As an aid in the prevention of coccidiosis caused by *E. necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. maxima*, and *E. mivati*; for increased rate of weight gain and improved feed efficiency.

(b) *Limitations.* Do not feed to laying chickens; feed continuously as sole ration; as monensin sodium provided by No. 000986 in § 510.600 of this chapter; virginiamycin provided by No. 000007 in § 510.600 of this chapter.

(xiv) *Amount per ton.* Monensin, 90 to 110 grams, plus 500 grams chlortetracycline.

(a) *Indications for use.* As an aid in the reduction of mortality due to *Escherichia coli* infections susceptible to such treatment. As an aid in the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*.

(b) *Limitations.* Do not feed to laying chickens; feed for 5 days as the sole ration; withdraw 24 hours before slaughter; in the absence of coccidiosis, the use of monensin with no withdrawal period may limit feed intake resulting in reduced weight gain; not to be fed continuously for more than 5 days; as monensin sodium; as chlortetracycline hydrochloride provided by No. 010042 in § 510.600(c) of this chapter.

(xv) *Amount per ton.* Monensin, 90 to 110 grams, plus bacitracin zinc, 10 grams, and roxarsone, 15 grams (0.0017 percent).

(a) *Indications for use.* For increase in rate of weight gain; for the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*.

(b) *Limitations.* Do not feed to laying chickens; feed continuously as the sole ration; withdraw 5 days before slaughter; as sole source of organic arsenic; feed must be used within 4 weeks of manufacture; as monensin sodium; as bacitracin zinc provided by No. 011716 in § 510.600(c) of this chapter; as roxarsone provided by No. 017210 in § 510.600(c) of this chapter.

(xvi) *Amount per ton.* Monen 1, 90 to 110 grams, plus bacitracin zinc, 4 to 50 grams, and roxarsone, 15 to 45.4 grams (0.0017 percent to 0.005 percent).

(a) *Indications for use.* For improved feed efficiency; for improved pigmentation by enhancing carotenoid and xanthophyll utilization; for the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*.

lina, *E. maxima*, *E. brunetti*, and *E. mivati*.

(b) *Limitations.* Do not feed to laying chickens; feed continuously as the sole ration; withdraw 5 days before slaughter; as sole source of organic arsenic; feed must be used within 4 weeks of manufacture; as monensin sodium; as bacitracin zinc provided by No. 011716 in § 510.600(c) of this chapter; as roxarsone provided by No. 017210 in § 510.600(c) of this chapter.

(xvii) *Amount per ton.* Monensin, 90 to 110 grams plus bambermycins, 1 to 2 grams plus roxarsone, 22.7 to 45.4 grams (0.0025 to 0.005 percent). See § 558.95(b)(1)(xiii) of this chapter.

(xviii) *Amount per ton.* Monensin, 90 to 110 grams, plus bacitracin methylene disalicylate, 50 grams, and roxarsone, 22.7 to 34.0 grams (0.0025 percent to .00375 percent).

(a) *Indications for use.* For increase in rate of weight gain and improved feed efficiency; as an aid in the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*; as an aid in the prevention of necrotic enteritis caused or complicated by *Clostridium* spp or other organisms susceptible to bacitracin methylene disalicylate.

(b) *Limitations.* Do not feed to laying chickens; feed continuously as the sole ration; withdraw 5 days before slaughter; as sole source of organic arsenic; as monensin sodium provided by No. 000986 in § 510.600(c) of this chapter; as bacitracin methylene disalicylate provided by No. 046573 in § 510.600(c) of this chapter; as roxarsone provided by No. 017210 in § 510.600(c) of this chapter.

(xix) *Amount per ton.* Monensin, 90 to 110 grams, plus bacitracin methylene disalicylate, 50 grams, and roxarsone, 22.7 to 45.4 grams (0.0025 percent to .005 percent).

(a) *Indications for use.* For increased rate of weight gain; as an aid in the prevention of necrotic enteritis caused or complicated by *Clostridium* spp or other organisms susceptible to bacitracin methylene disalicylate; as an aid in the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*.

(b) *Limitations.* Do not feed to laying chickens; feed continuously as the sole ration; withdraw 5 days before slaughter; as sole source of organic arsenic; as monensin sodium provided by No. 000986 in § 510.600(c) of this chapter; as bacitracin methylene disalicylate provided by No. 046573 in § 510.600(c) of this chapter; as roxarsone provided by No. 017210 in § 510.600(c) of this chapter.

(xx) *Amount per ton.* Monensin, 90 to 110 grams, plus virginiamycin, 5 to 15 grams, and roxarsone, 22.7 grams (0.0025 percent).

(a) *Indications for use.* For increase in rate of weight gain; as an aid in the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*.

(b) *Limitations.* Do not feed to laying chickens; feed continuously as the sole ration; withdraw 5 days before slaughter; as sole source of organic arsenic; as monensin sodium; as roxarsone provided by Nos. 017210 and 011801 in § 510.600(c) of this chapter.

(xxi) *Amount per ton.* Monensin, 90 to 110 grams, plus virginiamycin, 5 to 15 grams.

(a) *Indications for use.* For increase in rate of weight gain; as an aid in the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*.

(b) *Limitations.* Do not feed to laying chickens; feed continuously as sole ration; as monensin sodium provided by No. 000986 in § 510.600 of this chapter; virginiamycin provided by No. 000007 in § 510.600 of this chapter.

(xxii) *Amount per ton.* Monensin, 90 to 110 grams plus oxytetracycline, 500 grams.

(a) *Indications for use.* As an aid in the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*; as an aid in the reduction of mortality due to airsacculitis (air-sac infection) caused by *Escherichia coli* sensitive to oxytetracycline.

(b) *Limitations.* Feed for 5 days as sole ration. Do not feed to laying chickens. Withdraw 24 hours before slaughter. As monensin sodium provided by No. 000986 in § 510.600(c) of this

chapter. As mono-alkyl (C_8-C_{18}) trimethylammonium oxytetracycline provided by No. 000069 in § 510.600(c) of this chapter.

(xxiii) *Amount per ton.* Monensin, 90 to 110 grams, plus bacitracin zinc, 4 to 50 grams, and roxarsone, 22.7 to 45.4 grams (0.0025 percent to 0.005 percent).

(a) *Indications for use.* For improved feed efficiency; as an aid in the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*.

(b) *Limitations.* Do not feed to laying chickens; feed continuously as the sole ration; withdraw 5 days before slaughter; as sole source of organic arsenic; as monensin sodium provided by No. 000986 in § 510.600(c) of this chapter; as bacitracin zinc provided by No. 046573 in § 510.600(c) of this chapter; as roxarsone provided by No. 017210 in § 510.600(c) of this chapter.

(xxiv) *Amount per ton.* Monensin, 110 grams, plus bacitracin methylene disalicylate, 4 to 50 grams.

(a) *Indications for use.* For improved feed efficiency; as an aid in the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*.

(b) *Limitations.* Do not feed to laying chickens; feed continuously as the sole ration; in the absence of coccidiosis, the use of monensin with no withdrawal period may limit feed intake resulting in reduced weight gain; as monensin sodium provided by No. 000986 in § 510.600(c) of this chapter; as bacitracin methylene disalicylate provided by No. 046573 in § 510.600(c) of this chapter.

(2) *Turkeys*—(i) *Amount per ton.* Monensin, 54 to 90 grams.

(ii) *Indications for use.* For the prevention of coccidiosis in turkeys caused by *E. adenoides*, *E. meleagris*, and *E. gallopavonis*.

(iii) *Limitations.* Feed continuously as the sole ration from 1 day of age to 10 weeks of age; as monensin sodium; do not allow horses, other equines, mature turkeys, or guinea fowl access to feed containing monensin.

(3) *Cattle*—(i) *Amount per ton.* Monensin, 5-30 grams.

(a) *Indications for use.* Improved feed efficiency.

(b) *Limitations.* (1) Feed only to cattle being fed in confinement for slaughter. Feed continuously in complete feed at a rate of 50 to 360 milligrams of monensin per head per day; as monensin sodium. Complete feeds may be manufactured from monensin liquid Type B feeds. The liquid Type B feeds have a pH of 4.3 to 7.1 and their labels must bear appropriate mixing directions. Mixing directions for liquid Type B feeds stored in recirculating tank systems are: Recirculate immediately prior to use for no less than 10 minutes, moving not less than 1 percent of the tank contents per minute from the bottom of the tank to the top. Recirculate daily, as directed in this paragraph, even when Type B feed is not used. Mixing directions for liquid Type B feeds stored in mechanical, air, or other agitation-type tank systems are: Agitate immediately prior to use for not less than 10 minutes, creating a turbulence at the bottom of the tank that is visible at the top. Agitate daily, as directed in this paragraph, even when Type B feed is not used. The liquid Type B feed must bear directions to mix thoroughly with grain and/or roughage prior to feeding and must bear caution statements as follows: Inadequate mixing, (recirculation or agitation), of liquid Type B feeds has resulted in increased monensin concentration which has been fatal to cattle.

(2) An approved positionally stable monensin liquid Type B feed will not be subject to the requirements for mixing directions and cautionary labeling prescribed in paragraph (f)(3)(i)(b)(1) of this section. A manufacturer may secure approval of a positionally stable liquid Type B feed by (i) either filing an NADA for the product or by establishing a master file containing data to support the stability of its product; (ii) authorizing the agency to reference and rely upon the data in the master file to support approval of a supplemental NADA to establish positional stability; and (iii) requesting No. 000986 in § 510.600(c) of this chapter to file a supplemental NADA to provide for the use of its monensin Type A article in the manu-

facture of the liquid Type B feed specified in the appropriate master file. If the data demonstrate the stability of the liquid Type B feed described in the master file, the agency will approve the supplemental NADA. Approval of the Type B feed need not be published in the *FEDERAL REGISTER* because approval will not affect or alter the content of the regulation. The approval will, however, provide a basis for the individual liquid feed manufacturer to submit, and for the agency to approve, a medicated feed application under section 512(m) of the act for the liquid Type B feed. A manufacturer who seeks to market a positionally unstable monensin liquid Type B feed with mixing directions different from the standard established in paragraph (f)(3)(i)(b)(1) of this section may also follow this procedure.

(ii) *Amount per ton.* Monensin, 5 to 30 grams, plus tylosin, 8 to 10 grams.

(a) *Indications for use.* Improved feed efficiency; for reduction of incidence of liver abscesses caused by *Sphaerophorus necrophorus* and *Corynebacterium pyogenes*.

(b) *Limitations.* Feed only to cattle being fed in confinement for slaughter. Feed continuously as sole ration at the rate of 50 to 360 milligrams of monensin and 90 milligrams of tylosin per head per day; as monensin sodium; as tylosin phosphate.

(iii) *Amount per ton.* Monensin, 25 to 400 grams.

(a) *Indications for use.* Increased rate of weight gain.

(b) *Limitations.* Feed to pasture cattle (slaughter, stocker, feeder, and dairy and beef replacement heifers) weighing more than 400 pounds. Feed at the rate of not less than 50 nor more than 200 milligrams per head per day in not less than 1 pound of feed or, after the fifth day feed at the rate of 400 milligrams per head per day every other day in not less than 2 pounds of feed, as monensin sodium. During the first 5 days of feeding, cattle should receive no more than 100 milligrams per day.

(iv) *Amount per ton.* Monensin, 5 to 30 grams per ton (to provide 50 to 360 milligrams per head per day), plus melengestrol acetate, 0.25 to 1.6 grams

per ton (to provide 0.25 to 0.40 milligram per head per day).

(a) *Indications for use.* For increased rate of weight gain, improved feed efficiency, and suppression of estrus (heat).

(b) *Limitations.* Heifers being fed in confinement for slaughter: Administer melengestrol acetate and monensin by: (1) Adding melengestrol acetate from a separate Type B feed containing 0.125 to 0.8 milligram per pound to Type C medicated feeds containing monensin at 5 to 30 grams per ton, (2) adding melengestrol acetate from a separate Type B feed containing 0.125 to 0.8 milligram per pound and monensin from a separate Type B feed containing 50 to 1,200 grams per ton to Type C medicated feeds, (3) adding melengestrol acetate and monensin which are contained in the same dry Type B feed at the ranges in paragraph (f)(3)(iv)(b) (1) and (2) of this section to Type C medicated feeds, or (4) using a liquid Type B feed containing 0.125 to 0.8 milligram melengestrol acetate per pound and 25 to 600 milligrams monensin per pound (50 to 1,200 grams per ton) to make Type C medicated feeds. Type C medicated feeds in paragraph (f)(3)(iv)(b) (1) and (2) of this section may be manufactured from monensin liquid Type B feeds in accordance with paragraph (f)(3)(ix)(b) of this section. Withdraw melengestrol acetate 48 hours prior to slaughter.

(v) *Amount.* 150 milligrams per pound (0.033 percent).

(a) *Indications for use.* Increased rate of weight gain.

(b) *Limitations.* As protein-mineral blocks to be fed free choice to cattle (slaughter, stocker, feeder, and dairy and beef replacement heifers weighing more than 400 pounds) on pasture which may require supplemental feed. Provide 50 to 200 milligrams of monensin (0.34 to 1.33 pounds) per head per day, at least 1 block per 10 to 12 head of cattle. Roughage must be available at all times. Do not allow animals access to other protein blocks, salt or mineral, while being fed this product. Do not allow horses or other equines access to formulations containing monensin (ingestion of monensin by equines has been fatal). Block's

effectiveness in cull cows and bulls has not been established. Approval must comply with § 510.455 of this chapter.

(vi) *Amount per ton.* Monensin, 25 to 400 grams.

(a) *Indications for use.* Improved feeding efficiency for mature reproducing beef cows receiving supplemental feed.

(b) *Limitations.* Thoroughly mix the appropriate amount of Type A medicated article or Type B medicated feed with grain and roughage to provide a supplemental feed having a final concentration of 25 to 400 grams of monensin per ton. The final concentration should be contained in a minimum of 1 pound of feed. Either hand-feed or mix into the total ration. Feed continuously at a rate of not less than 50 nor more than 200 milligrams per head per day. During the first 5 days of feeding, cattle should receive no more than 100 milligrams per head per day.

(4) *Replacement chickens intended for use as cage layers—(i) Amount per ton.* Monensin, 90 to 110 grams.

(ii) *Indications for use.* As an aid in the prevention of coccidiosis caused by *E. necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*.

(iii) *Limitations.* Do not feed to laying chickens; feed continuously as sole ration; as monensin sodium; do not feed to chickens over 16 weeks of age.

(5) *Bobwhite quail—(i) Amount per ton.* Monensin, 73 grams.

(ii) *Indications for use.* For the prevention of coccidiosis in growing bobwhite quail caused by *Eimeria dispersa* and *E. lettyae*.

(iii) *Limitations.* Feed continuously as the sole ration; do not allow horses, other equines, mature turkeys, or guinea fowl access to feed containing monensin.

[40 FR 13950, Mar. 27, 1975]

EDITORIAL NOTE: FOR FEDERAL REGISTER citations affecting § 558.355, see the List of CFR Sections Affected in the Finding Aids section of this volume.

§ 558.360 Morantel tartrate.

(a) *Approvals.* Type A medicated articles: 88 grams per pound to 000060 in § 510.600(c) of this chapter.

(b) *Related tolerances.* See § 556.425 of this chapter.

(c) *Special considerations.* (1) Do not use in Type B or Type C medicated feeds containing bentonite.

(2) Consult your veterinarian before using in severely debilitated animals and for assistance in the diagnosis, treatment, and control of parasitism.

(d) *Conditions of use.*—(1) *Amount.* 0.44 to 4.4 grams of morantel tartrate per pound of feed.

(2) *Indications for use.* For removal and control of mature gastrointestinal nematode infections of cattle including stomach worms (*Haemonchus* spp., *Ostertagia* spp., *Trichostrongylus* spp.), worms of the small intestine (*Cooperia* spp., *Trichostrongylus* spp., *Nematodirus* spp.), and worms of the large intestine (*Oesophagostomum radiatum*).

(3) *Limitations.* Feed as a single therapeutic treatment at 0.44 gram of morantel tartrate per 100 pounds of body weight. Fresh water should be available at all times. When medicated feed is consumed, resume normal feeding. Conditions of constant worm exposure may require retreatment in 2 to 4 weeks. Do not treat animals within 14 days of slaughter.

FR 50950, Oct. 16, 1981, as amended at FR 53352, Nov. 26, 1982; 51 FR 7399, Mar. 1986; 51 FR 9005, Mar. 17, 1986; 52 FR 42, Apr. 10, 1987]

§ 558.363 Narasin.

(a) *Approvals.* Type A medicated articles containing the specified levels of narasin granted to firms identified by major numbers in § 510.600(c) of this chapter for use as in paragraph (c) of this section are as follows:

(1) To 000986: 36, 45, 54, 72, and 90 grams per pound, paragraph (c)(1)(i).

(2) To 000986: 36, 45, 54, 72, and 90 grams per pound with 10, 20, 50, and percent of roxarsone, paragraph (c)(1)(ii).

(3) To 000986: 36 grams per pound and 36 grams per pound of nicarbazine, paragraph (c)(1)(iii).

(4) To 012799: 36, 45, 54, 72, and 90 grams per pound with 2 and 10 grams per pound of bambamycin, paragraph (c)(1)(iv).

(b) *Tolerances.* See § 556.428 of this chapter.

(c) *Conditions of use.* It is used as follows:

(1) *Broiler chickens.*—(i) *Amount per ton.* Narasin, 54 to 72 grams.

(A) *Indications for use.* For prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*.

(B) *Limitations.* For broiler chickens only. Feed continuously as sole ration. Do not allow adult turkeys, horses, or other equines access to narasin formulations. Ingestion of narasin by these species has been fatal.

(ii) *Amount per ton.* Narasin, 54 to 72 grams, plus roxarsone 45.4 grams (0.005 percent).

(A) *Indications for use.* For the prevention of coccidiosis in broiler chickens caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati* including some field strains of *E. tenella* which are more susceptible to roxarsone combined with narasin than to narasin alone.

(B) *Limitations.* For broiler chickens only; feed continuously as the sole ration; do not feed to laying chickens; may be fatal if accidentally fed to adult turkeys or to horses; withdraw 5 days before slaughter; as sole source of organic arsenic; not approved for use with pellet binders.

(iii) *Amount per ton.* Narasin, 27 to 45 grams, plus nicarbazine, 27 to 45 grams.

(A) *Indications for use.* For the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*.

(B) *Limitations.* For broiler chickens only. Feed continuously as the sole ration. Do not feed to laying hens. Do not allow adult turkeys, horses, or other equines access to formulations containing narasin. Ingestion of narasin by these animals has been fatal. Withdraw 5 days before slaughter. The 2 drugs can be combined only at a 1:1 ratio for the 27 to 45 grams per ton range. Only granular nicarbazine as provided by No. 000986 in § 510.600(c) of this chapter may be used in the combination.

(iv) *Amount per ton.* Narasin, 54 to 72 grams, plus bambamycin, 1 to 2 grams.

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(A) *Indications for use.* For prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*, and for increased rate of weight gain and improved feed efficiency.

(B) *Limitations.* For broiler chickens only. Feed continuously as the sole ration. May be fatal if fed to adult turkeys, horses, or other equines.

(2) [Reserved]

[51 FR 29098, Aug. 14, 1986, as amended at 53 FR 24260, June 28, 1988; 54 FR 1928, Jan. 18, 1989; 54 FR 5930, Feb. 7, 1989; 54 FR 9430, Mar. 7, 1989]

§ 558.365 Nequinat.

(a) *Approvals.* Type A medicated articles: 4 percent to 017800 in § 510.600(c) of this chapter.

(b) *Related tolerances.* See § 556.440 of this chapter.

(c) *Special considerations.* Do not use in Type B or Type C medicated feeds containing bentonite.

(d) *Conditions of use.* It is used as follows:

(1) *Broiler or fryer chickens—(i) Amount per ton.* Nequinat, 18.16 grams.

(a) *Indications for use.* An aid in the prevention of coccidiosis caused by *E. tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*.

(b) *Limitations.* Feed continuously as the sole ration.

(ii) *Amount per ton.* Nequinat, 18.16 grams (0.002 percent) plus roxarsone, 45.4 grams (0.005 percent).

(a) *Indications for use.* An aid in the prevention of coccidiosis caused by *E. tenella*, *E. necatrix*, *E. acervulina*, *E.*

brunetti, and *E. mivati*; growth promotion and feed efficiency; for improving pigmentation.

(b) *Limitations.* Feed continuously as sole ration throughout the starting period; withdraw 5 days before slaughter; as sole source of organic arsenic.

(iii) *Amount per ton.* Nequinat, 18.16 grams (0.002 percent) plus oxytetracycline, 200 grams.

(a) *Indications for use.* For control of complicated chronic respiratory disease (air-sac infection), infectious synovitis, and treatment of blue comb (nonspecific infectious enteritis).

(b) *Limitations.* As monoalkyl ($C_{12}-C_{18}$) trimethylammonium oxytetracycline as provided by No. 000009 in § 510.600(c) of this chapter.

(2) *Roaster chickens or replacement chickens for caged layers—(i) Amount per ton.* Nequinat, 18.16 grams (0.002 percent).

(ii) *Indications for use.* An aid in the prevention of coccidiosis caused by *E. tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*.

(iii) *Limitations.* Feed continuously as the sole ration; do not feed to chickens over 16 weeks of age.

[40 FR 13959, Mar. 27, 1975, as amended at 51 FR 7399, Mar. 3, 1986; 52 FR 2683, Jan. 26, 1987]

§ 558.366 Nicarbazine.

(a) *Approvals.* Type A medicated articles: 25 percent to 000006 and 000906 in § 510.600(c) of this chapter.

(b) *Related tolerances.* See § 556.440 of this chapter.

(c) *Conditions of use.* It is used in chicken feed as follows:

Nicarbazine in grams per ton	Combination in grams per ton	Indications for use	Limitations	Spacer
27 to 45	Narsin 27 to 45	Broiler chickens; prevention of coccidiosis caused by <i>Eimeria tenella</i> , <i>E. necatrix</i> , <i>E. acervulina</i> , <i>E. maxima</i> , <i>E. brunetti</i> , and <i>E. mivati</i> .	Sec. 558.363 (c)(1)(ii)	000006
113.5 (0.0125 pct) ¹		Chickens; aid in preventing outbreaks of cecal (<i>Eimeria tenella</i>) and intestinal (<i>E. acervulina</i> , <i>E. maxima</i> , <i>E. necatrix</i> , and <i>E. brunetti</i>) coccidiosis. ¹	Feed continuously as sole ration from time chicks are placed on litter until past the time when coccidiosis is ordinarily a hazard; do not use as a treatment for coccidiosis; do not use in flushing fashers; do not feed to laying hens; withdraw 4 days before slaughter.	000006 000906

Resorbable in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
112.5 (0.0125 pct)	Lincomycin 2 (0.00044 pct).	Broiler chickens; aid in preventing outbreaks of cecai (<i>E. tenella</i>) and intestinal (<i>E. acervulina</i> , <i>E. maxima</i> , <i>E. necatrix</i> and <i>E. brunetti</i>) coccidiosis; for increased rate of weight gain.	do	000006
	Roxarsone 22.7 (0.0025).	do	Feed continuously as sole ration from time chicks are placed on litter until past the time when coccidiosis is ordinarily a hazard; as sole source of organic arsenic; do not use a treatment for coccidiosis; do not use in flushing meshes; do not feed to laying hens; withdraw 5 days before slaughter.	000006
	Roxarsone 22.7 (0.0025) plus lincomycin 2 (0.0004).	do	do	000006

These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data specified by § 514.111 of this chapter.

[42 FR 56729, Oct. 28, 1977; 43 FR 1942, Jan. 13, 1978, as amended at 44 FR 40887, July 13, 1979; 50 FR 13562, Apr. 5, 1985; 51 FR 7399, Mar. 3, 1986; 54 FR 1928, Jan. 18, 1989]

§ 558.367 Niclosamide.

(a) *Approvals*. Type A medicated articles: 66 percent to 000859 in § 510.600(c) of this chapter.

(b) *Conditions of use*. It is used in the feed of laboratory mice as follows:

(1) *Amount per ton*. 6.6 pounds (0.33 percent).

(2) *Indications for use*. Control of the mouse tapeworm *Hymenolepis* spp.

(3) *Limitations*. Feed daily for 7 consecutive days. Do not administer other drugs during treatment. If reinfection occurs, treatment may be repeated after 30 days. Do not feed to sick or debilitated animals or animals under severe stress. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism. When mixed according to directions and fed free choice, the feed will provide a daily dose of 500 milligrams per kilogram of body weight.

[PR 36810, Sept. 1, 1976, as amended at PR 7399, Mar. 3, 1986]

§ 558.369 Nitarsone.

(a) *Approvals*. Type A medicated articles: 50 percent to 017210 in § 510.600(c) of this chapter.

(b) *Related tolerances*. See § 556.60 of this chapter.

(c) *NAS/NRC status*. These conditions of use are NAS/NRC reviewed and found effective. NADA's for these uses may not require effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(d) *Conditions of use*. It is used for chickens and turkeys as follows:

(1) *Amount*. Nitarsone, 0.01875 percent.

(2) *Indications for use*. As an aid in the prevention of blackhead.

(3) *Limitations*. Early medication is essential to prevent spread of disease. Adequate drinking water must be provided near feeder at all times. The drug is not effective in preventing blackhead in birds infected more than 4 or 5 days. Discontinue use 5 days before slaughtering animals for human consumption to allow elimination of the drug from edible tissues. The drug is dangerous for ducks, geese, and dogs. Overdosage or lack of water may result in leg weakness or paralysis. Use as sole source of arsenic.

[46 FR 47535, Sept. 29, 1981, as amended at 47 FR 14152, Apr. 2, 1982; 51 FR 7399, Mar. 3, 1986; 52 FR 2686, Jan. 26, 1987]

§ 558.370

§ 558.370 Nitrofurazone.

(a) **Approvals.** Type A medicated articles: 50 grams per pound to 000007 and 011801 in § 510.600(c) of this chapter.

(b) **Conditions of use.** It is used for mink as follows:

(1) **Amount per ton.** 100 to 200 grams (0.011 to 0.022 percent).

(i) **Indications for use.** Treatment of gray diarrhea.

(ii) **Limitations.** Feed 100 grams per ton for 3 days, then 200 grams per ton for 21 days (amount of active ingredient calculated on feed before water added); do not repeat treatment. Discard unused mixed feed every 24 hours.

(2) **Amount per ton.** 100 grams (0.011 percent).

(i) **Indications for use.** Control of gray diarrhea.

(ii) **Limitations.** Feed continuously during susceptible period, not to exceed 90 days (amount of active ingredient calculated on feed before water added). Discard unused mixed feed every 24 hours.

[41 FR 11002, Mar. 15, 1976, as amended at 51 FR 7399, Mar. 3, 1986; 52 FR 2686, Jan. 26, 1987]

§ 558.376 Nitromide and sulfantran.

(a) **Approvals.** Type A medicated articles: 25 percent nitromide, 30 percent sulfantran, with or without 5 percent roxarsone to 017210 in § 510.600(c) of this chapter.

(b) **Related tolerances.** See §§ 556.220 and 556.680 of this chapter.

(c) **Conditions of use.** It is used for chickens as follows:

(1) **Amount.** 227 grams per ton nitromide (0.025 percent) and 272 grams per ton sulfantran (0.03 percent).

(i) **Indications for use.** As an aid in the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, and *E. acervulina*.

(ii) **Limitations.** Not to be fed to laying chickens; withdraw 5 days before slaughter; from Type A articles containing not more than 25 percent nitromide and 30 percent sulfantran.

(2) **Amount.** 227 grams per ton nitromide (0.025 percent) and 272 grams per ton sulfantran (0.03 percent), plus 45.4 grams per ton roxarsone (0.005 percent).

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(i) **Indications for use.** Prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, and *E. acervulina*; growth promotion and feed efficiency; improving pigmentation.

(ii) **Limitations.** Not to be fed to laying chickens; withdraw 5 days before slaughter; from Type A articles containing not more than 25 percent nitromide, 30 percent sulfantran, and 5 percent roxarsone; as sole source of organic arsenic.

[41 FR 11002, Mar. 15, 1976, as amended at 51 FR 7399, Mar. 3, 1986; 52 FR 2686, Jan. 26, 1987]

§ 558.415 Novobiocin.

(a) **Approvals.** Type A medicated articles: 25 grams of activity per pound to 000009 in § 510.600(c) of this chapter. Type B medicated feeds: 17.5 grams per pound to 000009 in § 510.600(c) of this chapter.

(b) **Related tolerances.** See § 556.400 of this chapter.

(c) **Conditions of use.** It is used in animal feeds as follows:

(1) **Chickens—(i) Amount.** Novobiocin, 6-7 mgs. per lb. body weight per day.

(a) **Indications for use.** Aid in the treatment of breast blisters associated with staphylococcal infections susceptible to novobiocin.

(b) **Limitations.** Administer, as sole ration, feed which contains not less than 200 grams of novobiocin activity per ton of feed; not for laying chickens; feed 5 to 7 days; withdraw 4 days before slaughter.

(ii) **Amount.** Novobiocin, 10-14 mgs. per lb. body weight per day.

(a) **Indications for use.** Treatment of staphylococcal synovitis and generalized staphylococcal infections susceptible to novobiocin.

(b) **Limitations.** Administer, as sole ration, feed which contains not less than 350 grams of novobiocin activity per ton of feed; not for laying chickens; feed 5 to 7 days; withdraw 4 days before slaughter.

(2) **Turkeys—(i) Amount.** Novobiocin, 4-5 mgs. per lb. body weight per day.

(a) **Indications for use.** Aid in the treatment of breast blisters associated with staphylococcal infections susceptible to novobiocin.

(b) *Limitations.* Administer, as sole ration, feed which contains not less than 200 grams of novobiocin activity per ton of feed; not for laying turkeys; feed 5 to 7 days; withdraw 4 days before slaughter.

(ii) *Amount.* Novobiocin, 5-8 mgs. per lb. body weight per day.

(a) *Indications for use.* Aid in the control of recurring outbreaks of fowl cholera caused by strains of *Pasteurella multocida* susceptible to novobiocin following initial treatment with 7-8 mgs. per pound body weight per day.

(b) *Limitations.* Administer, as sole ration, feed which contains not less than 200 grams of novobiocin activity per ton of feed; feed 5 to 7 days; not for laying turkeys; withdraw 4 days before slaughter.

(iii) *Amount.* Novobiocin, 7-8 mgs. per lb. body weight per day.

(a) *Indications for use.* Treatment of staphylococcal synovitis and generalized staphylococcal infection susceptible to novobiocin; treatment of acute outbreaks of fowl cholera caused by strains of *Pasteurella multocida* susceptible to novobiocin.

(b) *Limitations.* Administer, as sole ration, feed which contains not less than 350 grams of novobiocin activity per ton of feed; feed 5 to 7 days; not for laying turkeys; withdraw 4 days before slaughter.

(3) *Mink.*—(i) *Amount.* 20 mgs. per lb. body weight per day.

(ii) *Indications for use.* For treatment of generalized infections, abscesses, or urinary infections caused by staphylococcal or other novobiocin sensitive organisms.

(iii) *Limitations.* Administer, as sole ration, feed which contains not less than 200 grams of novobiocin activity per ton of feed; feed for 7 days.

(4) *Ducks.*—(i) *Amount.* Novobiocin, 50 grams per ton.

(ii) *Indications for use.* Control of infectious serositis and fowl cholera in ducks caused by *Pasteurella anatis* and *P. multocida*, susceptible to novobiocin.

(iii) *Limitations.* Administer, as sole ration, for 5 to 7 days, continue medication for 14 days if necessary, repeat if reinfection occurs; discontinue use at least 3 days before slaughter; not for use in laying ducks.

[40 FR 13959, Mar. 27, 1975, as amended at 45 FR 42263, June 24, 1980; 51 FR 7399, Mar. 3, 1986; 52 FR 36402, Sept. 29, 1987]

§ 558.430 Nystatin.

(a) *Approvals.* Type A medicated articles: 20 grams of activity per pound to 017210 in § 510.600(c) of this chapter.

(b) *Related tolerances.* See § 556.470 of this chapter.

(c) *Conditions of use.* It is used for chickens and turkeys as follows:

(1) *Amount.* 50 grams per ton.

(i) *Indications for use.* Chickens and turkeys; aid in control of crop mycosis and mycotic diarrhea (*Candida albicans*).

(ii) *Limitations.* Growing and laying chickens; growing turkeys.

(2) *Amount.* 100 grams per ton.

(i) *Indications for use.* Chickens and turkeys; treatment of crop mycosis and mycotic diarrhea (*Candida albicans*).

(ii) *Limitations.* Growing and laying chickens; growing turkeys; to be fed for 7 to 10 days.

[41 FR 11002, Mar. 15, 1976, as amended at 51 FR 7399, Mar. 3, 1986; 52 FR 2686, Jan. 26, 1987; 53 FR 40729, Oct. 18, 1988]

§ 558.435 Oleandomycin.

(a) *Approvals.* Type A medicated articles: 5 grams of activity per pound to 000069 in § 510.600(c) of this chapter.

(b) *Related tolerances.* See § 556.480 of this chapter.

(c) *Special considerations.* Do not use bentonite in Type B or Type C medicated feeds containing oleandomycin. Oleandomycin refers to oleandomycin or feed-grade oleandomycin.

(d) *Conditions of use.* It is used in animal feed as follows:

(1) *Chickens and turkeys.*—(i) *Amount per ton.* Oleandomycin, 1 to 2 grams.

(ii) *Indications for use.* For increased rate of weight gain and improved feed efficiency for broiler chickens and growing turkeys.

(2) *Swine.*—(i) *Amount per ton.* Oleandomycin, 5 to 11.25 grams.

(ii) *Indications for use.* For increased rate of weight gain and improved feed efficiency in growing-finishing swine.

§ 558.450

[40 FR 13959, Mar. 27, 1975, as amended at 44 FR 40283, July 10, 1979; 51 FR 7399, Mar. 3, 1986; 52 FR 2686, Jan. 26, 1987]

§ 558.450 Oxytetracycline.

(a) *Approvals.* Type A medicated articles: (1) 10 and 50 grams per pound to 000089 in § 510.600(c) of this chapter for use as in paragraph (d) of this section.

(2) 100 grams per pound to 000089 in § 510.600(c) of this chapter for use as

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in paragraph (d)(1), table 1, item (v) and table 3, item (ii) of this section.

(b) *Special considerations.* The amount of mono-alkyl (C_8-C_{12}) trimethylammonium oxytetracycline is expressed in terms of an equivalent amount of oxytetracycline hydrochloride.

(c) *Related tolerances.* See § 556.500 of this chapter.

(d) *Conditions of use.* (1) It is used as follows:

TABLE 1—IN CHICKEN AND TURKEY FEED

Oxytetracycline in grams per ton	Combination in grams per ton	Indications for use	Limitations	Expiry
(i) 50		Chickens and turkeys; during times of stress, for prevention of diseases named in this section caused by organisms susceptible to the named levels of the oxytetracycline salt.	As mono-alkyl (C_8-C_{12}) trimethyl ammonium oxytetracycline.	
(ii) 50 to 100		1. Chickens; prevention of blue comb (nonspecific infectious enteritis). 2. Chickens and turkeys; prevention of early mortality of chicks and poults due to organisms susceptible to the oxytetracycline salt. 3. Turkeys; prevention of hexamitiasis.	—do— For chicks (1st 2 weeks of life); for poults (1st 4 weeks of life); as mono-alkyl (C_8-C_{12}) trimethyl ammonium oxytetracycline. As mono-alkyl (C_8-C_{12}) trimethyl ammonium oxytetracycline.	
(iii) 100-200		1. Chickens; prevention of complicated chronic respiratory disease (air-sac infection) and control of complicated chronic respiratory mortality and severity during outbreaks; prevention of fowl cholera. 2. Chickens; treatment of blue comb (nonspecific infectious enteritis); prevention of infectious synovitis; control of complicated chronic respiratory disease (air-sac infection) by lowering mortality and severity of disease during outbreaks; reduction of lesion and mortality due to organisms susceptible to oxytetracycline in the presence of complicated chronic respiratory disease (air-sac infection). 3. Turkeys; control of infectious sinusitis; prevention of infectious synovitis. 4. Turkeys; control blue comb (nonspecific infectious enteritis, mud fever); treatment of hexamitiasis.	—do— As mono-alkyl (C_8-C_{12}) trimethyl ammonium oxytetracycline in low-calcium feed containing 0.18% to 0.55% dietary calcium; not to be fed continuously for more than 5 d; low calcium feeds may be fed for a total of 3 5-d periods through the 1st 10 weeks of life with an interim period of 5 d between each low-calcium feeding. Not to be fed to laying chickens. As mono-alkyl (C_8-C_{12}) trimethyl ammonium oxytetracycline. —do—	
(iv) 200		1. Turkeys; control of infectious synovitis.	As mono-alkyl (C_8-C_{12}) trimethyl ammonium oxytetracycline.	

TABLE 1—IN CHICKEN AND TURKEY FEED—Continued

Oxytetracycline in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
		2. Chickens; prevention of avian infectious hepatitis; prevention and control of <i>E. tenella</i> , cause of cecal coccidiosis.	As mono-alkyl (C ₉ —C ₁₃) trimethyl ammonium oxytetracycline in low-calcium feed containing 0.18% to 0.55% dietary calcium; not to be fed continuously for more than 5 d; low-calcium feeds may be fed for a total of 3 5-d periods through the 1st 10 weeks of life with an interim period of 5 d between each low-calcium feeding. Not to be fed to laying chickens.	
		3. Chickens; control of infectious synovitis.	As mono-alkyl (C ₉ —C ₁₃) trimethyl ammonium oxytetracycline.	
		4. Chickens; control of fowl cholera during periods of outbreaks.	As mono-alkyl (C ₉ —C ₁₃) trimethyl ammonium oxytetracycline; in low-calcium feed containing 0.18% to 0.55% dietary calcium; for 2 weeks from outbreak of disease, 5 d of low calcium and the remaining period on normal calcium; not to be fed to laying chickens.	
	Monensin 90 to 110.....	Broiler chickens; for the control of complicated chronic respiratory disease (CRD or air-sac infection) caused by <i>Mycoplasma gallisepticum</i> and <i>Escherichia coli</i> ; and as an aid in the prevention of coccidiosis caused by <i>Eimeria necatrix</i> , <i>E. tenella</i> , <i>E. acervulina</i> , <i>E. brunetti</i> , <i>E. mivati</i> , and <i>E. maxima</i> .	Do not feed to laying chickens; feed continuously as sole ration; as monensin sodium.	000069
	Nequinato 18.18 (0.002%).	Broiler or fryer chickens; as an aid in prevention of coccidiosis caused by <i>Eimeria tenella</i> , <i>E. necatrix</i> , <i>E. acervulina</i> , <i>E. maxima</i> , <i>E. brunetti</i> and <i>E. mivati</i> . For control of complicated chronic respiratory disease (air-sac infections), infectious synovitis, and treatment of blue comb (nonspecific infectious enteritis).	As monoalkyl (C ₉ —C ₁₃) trimethyl ammonium oxytetracycline. As mono-alkyl (C ₉ —C ₁₃) trimethyl ammonium oxytetracycline.	
500.....		Broiler chickens; as an aid in the reduction of mortality due to air-sacculitis (air-sac-infection) caused by <i>Escherichia coli</i> sensitive to oxytetracycline.	Feed for 5 d as sole ration; treat at first clinical signs of disease; do not feed to laying hens; withdraw 24 h prior to slaughter. As mono-alkyl (C ₉ —C ₁₃) trimethyl ammonium oxytetracycline.	000069

TABLE 1—IN CHICKEN AND TURKEY FEED—Continued

Oxytetracycline in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
	Monensin 90 to 110.....	Broiler chickens; as an aid in the reduction of mortality due to airsacculitis (air-sac infection) caused by <i>Escherichia coli</i> sensitive to oxytetracycline; as an aid in the prevention of coccidiosis caused by <i>Eimeria necatrix</i> , <i>E. tenella</i> , <i>E. acervulina</i> , <i>E. brunetti</i> , <i>E. mivati</i> , and <i>E. maxima</i> .	Feed for 5 days as sole ration; do not feed to laying chickens; withdraw 24 hours before slaughter. As mono-alkyl (C ₈ —C ₁₃) trimethyl ammonium oxytetracycline.	

TABLE 2—IN CATTLE FEED

Oxytetracycline in milligrams per head per day	Indications for use	Limitations	Sponsor
75 to 80.....	Beef cattle; reduction of the incidence and severity of liver abscesses.	For beef cattle weighing over 400 lb; as mono-alkyl (C ₈ —C ₁₃) trimethyl ammonium oxytetracycline.	

TABLE 3—IN FISH FEED

Oxytetracycline	Combination	Indications for use	Limitations	Sponsor
(i) 250 mg per kilogram of fish per day (11.35 g per 100 lb of fish per day).		Pacific salmon; for marking of skeletal tissue.	For salmon not over 30 g body weight; administer as sole ration for 4 consecutive days in feed containing oxytetracycline hydrochloride or mono-alkyl (C ₈ —C ₁₃) trimethyl ammonium oxytetracycline; fish not to be liberated for at least 7 d following the last administration of medicated feed.	
(ii) 2.5 to 3.75 g per 100 lb of fish per day.		1. Salmonids; control of ulcer disease caused by <i>Hemophilus piscium</i> , furunculosis caused by <i>Aeromonas salmonicida</i> , bacterial hemorrhagic septicemia caused by <i>Aeromonas liquefaciens</i> , and pseudomonas disease. 2. Catfish; control of bacterial hemorrhagic septicemia caused by <i>Aeromonas liquefaciens</i> and pseudomonas disease.	Administer as mono-alkyl (C ₈ —C ₁₃) trimethyl ammonium oxytetracycline in mixed ration for 10 d; do not liberate fish or slaughter fish for food for 21 d following the last administration of medicated feed; do not administer when water temperature is below 9° C (48.2° F). Administer as mono-alkyl (C ₈ —C ₁₃) trimethyl ammonium oxytetracycline in mixed ration for 10 d; do not liberate fish or slaughter fish for food for 21 d following the last administration of medicated feed; do not administer when water temperature is below 16.7° C (62° F).	
(iii) 1 g per lb of medicated feed.		Lobsters; control of gaffkemia caused by <i>Aerococcus viridans</i> .	Administer as sole ration for 5 consecutive days in feed containing monoalkyl (C ₈ —C ₁₃) trimethyl ammonium oxytetracycline; withdraw medicated feed 30 days before harvesting lobsters.	000000

(2) Oxytetracycline may be used in accordance with the provisions of this section in the combinations provided as follows:

- (i) Robenidine hydrochloride in accordance with § 558.515.
- (ii) Lasalocid as in § 558.311.

[41 FR 11002, Mar. 15, 1976, as amended at 41 FR 28514, July 12, 1976; 41 FR 47425, Oct. 29, 1976; 47 FR 51563, Nov. 16, 1982; 50 FR 42012, Oct. 17, 1985; 51 FR 7399, Mar. 3, 1986; 51 FR 16676, May 6, 1986; 52 FR 2686,

Jan. 26, 1987; 52 FR 24293, June 30, 1987; 52 FR 26401, July 14, 1987; 52 FR 48096, Dec. 18, 1987; 53 FR 27006, July 18, 1988]

§ 558.460 Penicillin.

(a) *Specifications.* As penicillin procaine G or feed grade penicillin procaine.

(b) *Related tolerances.* See § 556.510 of this chapter.

(c) *Conditions of use.* (1) It is used as follows:

Penicillin in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
(i) 1.5 to 42.5	Streptomycin 7.5 to 48.5	Swine; growth promotion and feed efficiency.	Feed not more than 50 g of combination containing at least 1.5 g of penicillin and at least 7.5 g of streptomycin; as streptomycin sulfate.	
(ii) 2.4 to 38.0	Streptomycin 12.0 to 47.6	Chickens and turkeys; growth promotion and feed efficiency.	Feed not more than 50 g of combination containing at least 2.4 g of penicillin and at least 12 g of streptomycin; as streptomycin sulfate.	
(iii) 2.4 to 50		Chickens, turkeys, and pheasants; growth promotion and feed efficiency.		
(iv) 5 to 20		Quail; growth promotion and feed efficiency.	Quail, not over 5 weeks of age.	
(v) 10 to 50		Swine; growth promotion and feed efficiency.		
(vi) 22.5 to 50 (of the combination)	Streptomycin	Chickens; maintaining or increasing egg production.	Feed contains 16.7% of penicillin; as procaine penicillin, as streptomycin sulfate.	
(vii) 45 to 90 (of the combination)	do	Swine; aid in the prevention of bacterial swine enteritis.	do	
(viii) 50 to 100		1. Chickens; prevention of chronic respiratory disease (air-sac infection), blue comb (nonspecific infectious enteritis).		
		2. Turkeys; prevention of infectious sinusitis, blue comb (mud fever).		
(ix) 90 (of the combination)	Streptomycin	1. Chickens; prevention of early mortality caused by organisms susceptible to penicillin and streptomycin.	For chicks; in starter ration containing 16.7% of penicillin; as procaine penicillin, as streptomycin sulfate.	
		2. Swine; treatment of bacterial swine enteritis.	Feed contains 16.7% of penicillin; as procaine penicillin, as streptomycin sulfate.	
(x) 90 to 180 (of the combination)	do	1. Chickens; treatment of chronic respiratory disease (air-sac infection), blue comb (nonspecific infectious enteritis).	do	
		2. Turkeys; treatment of infectious sinusitis; blue comb (mud fever), hexamitiasis.	do	
(xi) 90 to 270 (of the combination)	do	Swine; treatment of bacterial swine enteritis.	Feed contains 16.7% of penicillin; feed not more than 14 d; as procaine penicillin; as streptomycin sulfate.	
(xii) 100		1. Chickens; treatment of chronic respiratory disease (air-sac infection), blue comb (nonspecific enteritis).		

Penicillin in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
		2. Turkeys; treatment of infectious sinusitis, blue comb (mud fever).		

(2) Penicillin may be used in accordance with the provisions of this section in the combinations provided as follows:

- (i) Amprolium in accordance with § 558.55.
- (ii) Amprolium plus ethopabate in accordance with § 558.58.
- (iii)—(iv) [Reserved]
- (v) Buquinolate in accordance with § 558.105.
- (vi) Hygromycin B in accordance with § 558.274.
- (vii) [Reserved]
- (viii) Reserpine in accordance with § 558.505.
- (ix) Roxarsone and zoalene in accordance with § 558.680.
- (x) Zualene in accordance with § 558.680.

[41 FR 11004, Mar. 15, 1976, as amended at 42 FR 18618, Apr. 8, 1977; 42 FR 36995, July 19, 1977; 47 FR 42103, Sept. 24, 1982; 51 FR 7399, Mar. 3, 1986; 52 FR 2686, Jan. 26, 1987]

§ 558.464 Poloxalene.

(a) *Approvals.* (1) Dry Type A medicated articles: 53 percent to 000007 in § 510.600(c) of this chapter.

(2) Liquid Type A medicated articles: 99.5 percent to 000007 in § 510.600(c) of this chapter.

(b) *Conditions of use.* (1) For prevention of legume (alfalfa, clover) and wheat pasture bloat in cattle.

(2) Poloxalene dry Type A article and liquid Type A article must be thoroughly blended and evenly distributed in feed prior to use. This may be accomplished by adding the Type A article to a small quantity of feed, mixing thoroughly, then adding this mixture to the remaining feed and again mixing thoroughly. Dosage is 1 gram of poloxalene per 100 pounds of body weight daily and continued during exposure to bloat producing conditions. If bloating conditions are severe, the dose is doubled. Treatment should be started 2 to 3 days before exposure to bloat-producing condi-

tions. Repeat dosage if animals are exposed to bloat-producing conditions more than 12 hours after the last treatment. Do not exceed the higher dosage levels in any 24-hour period.

[40 FR 39857, Aug. 29, 1975, as amended at 51 FR 7399, Mar. 3, 1986; 52 FR 2686, Jan. 26, 1987]

§ 558.465 Poloxalene free-choice liquid Type C feed.

(a) *Approvals.* Type A medicated articles: 99.5 percent to 000007 in § 510.600(c) of this chapter.

(b) *Conditions of use.* (1) For control of legume (alfalfa, clover) and wheat pasture bloat in cattle, use 7.5 grams of poloxalene per pound of liquid Type C feed (1.65 percent weight/weight). Each animal must consume 0.2 pound of Type C feed per 100 pounds of body weight daily for adequate protection.

(2) For control of legume (alfalfa, clover) bloat in cattle grazing of prebloom legumes, use 10.00 grams of poloxalene per pound of liquid Type C feed (2.2 percent weight/weight). Each animal must consume 0.15 pound of Type C feed per 100 pounds of body weight daily for adequate protection. If consumption exceeds 0.2 pound of Type C feed per 100 pounds of body weight daily, cattle should be changed to a Type C feed containing 7.5 grams of poloxalene per pound.

(3) Poloxalene liquid Type A article must be thoroughly blended and evenly distributed into a liquid Type C feed and offered to cattle in a covered liquid Type C feed feeder with slick wheels. The formula for the liquid Type C feed, on a weight/weight basis, is as follows: Ammonium polyphosphate 2.66 percent, phosphoric acid (75 percent) 3.37 percent, sulfuric acid 1.00 percent, water 10.00 percent, and molasses sufficient to make 100.00 percent, vitamins A and D and/or trace minerals may be added. One free-turn-

lick wheel per 25 head of cattle must be provided.

(4) The medicated liquid Type C feed must be introduced at least 2 to 5 days before legume consumption to acustom the cattle to the medicated liquid Type C feed and to lick wheel feedings. If the medicated liquid wheel Type C feed feeding is interrupted, this 2- to 5-day introductory feeding should be repeated.

FR 13959, Mar. 27, 1975, as amended at FR 21281, Apr. 26, 1977; 51 FR 7399, Mar. 1986; 53 FR 2686, Jan. 26, 1987]

§ 558.485 Pyrantel tartrate.

(a) *Approvals.* Type A medicated articles containing pyrantel tartrate to be identified by drug labeler codes § 510.600(c) of this chapter for the specific usage indicated in paragraph (b) of this section:

(1) To 000069: 9.6, 19.2, and 80 grams per pound, paragraphs (e) (1) through (4) of this section.

(2) To 017800: 19.2 and 48 grams per pound, paragraphs (e) (1) through (3) of this section.

(3) To 016968: 9.6 and 19.2 grams per pound, paragraphs (e) (1) through (3) of this section.

(4) To 026186: 9.6 and 19.2 grams per pound, paragraphs (e) (1) through (3) of this section.

(5) To 017790: 9.6 and 19.2 grams per pound, paragraphs (e) (1) through (3) of this section.

(6) To 018083: 9.6 and 19.2 grams per pound, paragraphs (e) (1) through (3) of this section.

(7) To 051359: 9.6 and 19.2 grams per pound, paragraphs (e) (1) through (3) of this section.

(8) To 011490: 9.6 and 19.2 grams per pound, paragraphs (e) (1) through (3) of this section.

(9) To 011749: 9.6 and 19.2 grams per pound, paragraphs (e) (1) through (3) of this section.

(10) To 043733: 9.6 and 19.2 grams per pound, paragraphs (e) (1) through (3) of this section.

(11) To 017274: 9.6 and 19.2 grams per pound, paragraphs (e) (1) through (3) of this section.

(12) To 046987: 9.6 and 19.2 grams per pound, paragraphs (e) (1) and (2) of this section.

(13) To 034936: 9.6 and 19.2 grams per pound, paragraphs (e) (1) and (2) of this section.

(14) To 021810: 9.6 grams per pound, paragraphs (e) (1) through (3) of this section.

(15) To No. 049685: 9.6 and 19.2 grams per pound, paragraphs (e) (1) through (3) of this section.

(16) To No. 012190: 9.6 and 19.2 grams per pound, paragraphs (e) (1) through (3) of this section.

(17) To No. 047427: 9.6 and 19.2 grams per pound, paragraphs (e) (1) and (2) of this section.

(18) To No. 001800: 9.6 grams per pound, paragraphs (e) (1) through (3) of this section.

(19) To 050568: 9.6 and 19.2 grams per pound, paragraphs (e) (1) through (3) of this section.

(20) To 050639: 9.6 and 19.2 grams per pound, paragraphs (e) (1) through (3) of this section.

(21) To 043734: 9.6 and 19.2 grams per pound, paragraphs (e) (1) through (3) of this section.

(22) To 017473: 9.6 and 19.2 grams per pound, paragraphs (e) (1) through (3) of this section.

(23) To 021676: 19.2 grams per pound, paragraphs (e) (1) through (3) of this section.

(24) [Reserved]

(25) To 020275: 9.6 and 19.2 grams per pound, paragraphs (e) (1) through (3) of this section.

(26) [Reserved]

(27) To 010439: 9.6 and 19.2 grams per pound, paragraphs (e) (1) through (3) of this section.

(b) [Reserved]

(c) *Related tolerances.* See § 556.560 of this chapter.

(d) *Special considerations.* (1) Consult veterinarian before using in severely debilitated animals.

(2) Do not mix in Type B or Type C medicated feeds containing bentonite.

(e) *Conditions of use.* It is used in feed for swine as follows:

(1) *Amount per ton.* 96 grams (0.0106 percent).

(i) *Indications for use.* Aid in the prevention of migration and establishment of large roundworm (*Ascaris suum*) infections; aid in the prevention of establishment of nodular worm (*Oesophagostomum*) infections.

(ii) *Limitations.* Feed continuously as the sole ration in a Type C feed; withdraw 24 hours prior to slaughter.

(2) *Amount per ton.* 96 grams (0.0106 percent).

(i) *Indications for use.* For the removal and control of large roundworm (*Ascaris suum*) infections.

(ii) *Limitations.* Feed for 3 days as the sole ration in a Type C feed; withdraw 24 hours prior to slaughter.

(3) *Amount per ton.* 800 grams (0.0881 percent).

(i) *Indications for use.* For the removal and control of large roundworm (*Ascaris suum*) and nodular worm (*Oesophagostomum*) infections.

(ii) *Limitations.* As sole ration for a single therapeutic treatment in Type C feed; feed at the rate of 1 lb of feed per 40 lb of body weight for animals up to 200 lb, and 5 lb of feed per head for animals 200 lb or over; withdraw 24 hours prior to slaughter.

(4) *Amount per ton.* Pyrantel tartrate, 96 grams (0.0106 percent) and carbadox, 50 grams (0.0055 percent).

(i) *Indications for use.* For control of swine dysentery (vibronic dysentery, bloody scours or hemorrhagic dysentery); control of bacterial swine enteritis (salmonellosis or necrotic enteritis caused by *Salmonella choleraesuis*); aid in the prevention of migration and establishment of large roundworm (*Ascaris suum*) infections; aid in the prevention of establishment of nodular worm (*Oesophagostomum*) infections.

(ii) *Limitations.* Do not feed to swine weighing over 75 pounds; do not feed within 10 weeks of slaughter; consult a veterinarian before feeding to severely debilitated animals; feed continuously as sole ration. Do not use in Type C feeds containing less than 15 percent crude protein.

(5) *Amount per ton.* Pyrantel tartrate, 96 grams (0.0106 percent) and tylosin, 40 to 100 grams, as tylosin phosphate.

(i) *Indications for use.* For prevention of swine dysentery (vibronic); aid in the prevention of migration and establishment of large roundworms (*Ascaris suum*) infections; aid in the prevention of establishment of nodular worm (*Oesophagostomum* spp.) infections.

(ii) *Limitations.* Use 100 grams tylosin per ton for at least 3 weeks followed by 40 grams tylosin per ton until market weight; withdraw 24

hours before slaughter. Consult your veterinarian before feeding to severely debilitated animals and for assistance in the diagnosis, treatment, and control of parasitism.

(6) *Amount per ton.* Pyrantel tartrate, 96 grams (0.0106 percent) and tylosin 40 to 100 grams, as tylosin phosphate.

(i) *Indications for use.* Treatment and control of swine dysentery (vibronic); aid in the prevention of migration and establishment of large roundworm (*Ascaris suum*) infections; aid in the prevention of establishment of nodular worm (*Oesophagostomum* spp.) infections.

(ii) *Limitations.* Administer tylosin in feed as tylosin phosphate after treatment with tylosin in drinking water as tylosin base; 0.25 grams per gallon in drinking water for 3 to 10 days, 40 to 100 grams tylosin per ton in feed for 2 to 6 weeks; withdraw 24 hours before slaughter. Consult your veterinarian before feeding to severely debilitated animals and for assistance in the diagnosis, treatment, and control of parasitism.

(7) *Amount per ton.* Pyrantel tartrate, 96 grams (0.0106 percent) and lincomycin, 40 grams, as lincomycin hydrochloride monohydrate.

(i) *Indications for use.* For control of swine dysentery; aid in the prevention of migration and establishment of large roundworm (*Ascaris suum*) infections; aid in the prevention of establishment of nodular worm (*Oesophagostomum* spp.) infections.

(ii) *Limitations.* Feed as sole ration for use in swine on premises with a history of swine dysentery but where symptoms have not yet occurred; not to be fed to swine that weigh more than 250 pounds; withdraw 6 days before slaughter. Consult your veterinarian before feeding to severely debilitated animals and for assistance in the diagnosis, treatment, and control of parasitism.

(8) *Amount per ton.* Pyrantel tartrate, 96 grams (0.0106 percent) and lincomycin, 100 grams, then 40 grams, as lincomycin hydrochloride monohydrate.

(i) *Indications for use.* For treatment and control of swine dysentery; aid in the prevention of migration and

establishment of large roundworm (*Ascaris suum*) infections; aid in the prevention of establishment of nodular worm (*Oesophagostomum* spp.) infections.

(ii) *Limitations*. Feed 100 grams per ton for 3 weeks or until signs of disease disappear, followed by 40 grams per ton; feed as sole ration; not to be fed to swine that weigh more than 250 pounds; withdraw 6 days before slaughter. Consult your veterinarian before feeding to severely debilitated animals and for assistance in the diagnosis, treatment, and control of parasitism.

(9) *Amount per ton*. Pyrantel tartrate, 96 grams (0.0106 percent) and lincomycin, 100 grams, as lincomycin hydrochloride monohydrate.

(i) *Indications for use*. For treatment of swine dysentery; aid in the prevention of migration and establishment of large roundworm (*Ascaris suum*) infections; aid in the prevention of establishment of nodular worm (*Oesophagostomum* spp.) infections.

(ii) *Limitations*. Feed 100 grams per ton for 3 weeks or until signs of disease disappear, followed by 40 grams per ton; feed as sole ration; not to be fed to swine that weigh more than 250 pounds; withdraw 6 days before slaughter. Consult your veterinarian before feeding to severely debilitated animals and for assistance in the diagnosis, treatment, and control of parasitism.

(10) *Amount per ton*. Pyrantel tartrate, 96 grams (0.0106 percent) and lincomycin, 100 or 40 grams.

(i) *Indications for use*. For treatment and/or control of swine dysentery; for removal and control of large roundworm (*Ascaris suum*) infections.

(ii) *Limitations*. Administer in accordance with paragraph (c)(2)(i), (ii), or (iii) of § 558.325 and paragraph (e)(3)(i) of this section.

(1) *Amount per ton*. Pyrantel tartrate, 800 grams (0.0881 percent) and lincomycin, 100 or 40 grams.

(i) *Indications for use*. For treatment and/or control of swine dysentery for removal and control of large roundworm (*Ascaris suum*) and nodular worm (*Oesophagostomum* spp.) infections.

(ii) *Limitations*. Administer in accordance with paragraph (c)(2)(i), (ii), or (iii) of § 558.325 and paragraph (e)(3)(ii) of this section.

(12) *Amount per ton*. Pyrantel tartrate, 96 grams (0.0106 percent) and lincomycin, 200 grams as lincomycin hydrochloride monohydrate.

(i) *Indications for use*. For the reduction in severity of swine mycoplasma pneumonia caused by *Mycoplasma hyopneumoniae*; aid in the prevention of migration and establishment of large roundworms (*Ascaris suum*) infections; aid in the prevention of establishment of nodular worm (*Oesophagostomum* spp.) infections.

(ii) *Limitations*. Feed as sole ration for 21 days; not to be fed to swine that weigh more than 250 pounds; withdraw 6 days before slaughter; consult your veterinarian before feeding to severely debilitated animals and for assistance in the diagnosis, treatment, and control of parasitism.

(iii) *Sponsor*. See No. 000009 in § 510.600(c) of this chapter.

[40 FR 13959, Mar. 27, 1975]

EDITORIAL NOTE: For FEDERAL REGISTER citations affecting § 558.485, see the List of CFR Sections Affected in the Finding Aids section of this volume.

§ 558.515 Robenidine hydrochloride.

(a) *Approvals*. Type A medicated articles: 30 grams per pound to 010042 in § 510.600(c) of this chapter.

(b) *Special considerations*. Type C feed containing robenidine hydrochloride must be fed within 50 days from the date of manufacture. Do not use in Type B or Type C medicated feeds containing bentonite.

(c) *Related tolerances in edible products*. See § 556.580 of this chapter.

(d) *Conditions of use*. It is used in feed for chickens as follows:

(1) *For broiler and fryer chickens—*

(i) *Amount per ton*. Robenidine hydrochloride, 30 grams (0.0033 percent).

(a) *Indications for use*. As an aid in the prevention of coccidiosis caused by *E. mivati*, *E. brunetti*, *E. tenella*, *E. acervulina*, *E. maxima*, and *E. necatrix*.

(b) *Limitations*. Do not feed to layers; feed continuously as the sole

ration; withdraw 5 days prior to slaughter.

(ii) *Amount per ton.* Robenidine hydrochloride, 30 grams (0.0033 percent) plus roxarsone, 22.5-45.4 grams (.005 percent).

(a) *Indications for use.* As an aid in the prevention of coccidiosis caused by *E. mivati*, *E. brunetti*, *E. tenella*, *E. acervulina*, *E. maxima*, and *E. necatrix* and increased rate of weight gain.

(b) *Limitations.* Do not feed to layers; feed continuously as the sole ration; withdraw 5 days prior to slaughter; as sole source of organic arsenic. Roxarsone provided by No. 017210, § 510.600(c) of this chapter.

(iii) *Amount per ton.* Robenidine hydrochloride, 30 grams (0.0033 percent) plus chlortetracycline, 100 grams.

(a) *Indications for use.* As an aid in the prevention of coccidiosis caused by *E. mivati*, *E. brunetti*, *E. tenella*, *E. acervulina*, *E. maxima*, and *E. necatrix*; as an aid in the control of chronic respiratory disease (CRD) caused by *M. gallisepticum* susceptible to chlortetracycline; as an aid in the control of infectious synovitis caused by *M. synoviae* susceptible to chlortetracycline.

(b) *Limitations.* For broiler or fryer chickens only; withdraw 5 days prior to slaughter; do not feed to layers, feed continuously as sole ration; as chlortetracycline hydrochloride provided by No. 010042, § 510.600(c) of this chapter.

(iv) *Amount per ton.* Robenidine hydrochloride, 30 grams (0.0033 percent) plus chlortetracycline, 200 grams.

(a) *Indications for use.* As an aid in the prevention of coccidiosis caused by *E. mivati*, *E. brunetti*, *E. tenella*, *E. acervulina*, *E. maxima*, and *E. necatrix*; as an aid in the treatment of infectious synovitis caused by *M. synoviae* susceptible to chlortetracycline; as an aid in the control of chronic respiratory disease (CRD) caused by *M. gallisepticum* susceptible to chlortetracycline.

(b) *Limitations.* Withdraw 5 days prior to slaughter; do not feed to layers; feed continuously as sole ration; as chlortetracycline hydrochloride provided by No. 010042, § 510.600(c) of this chapter.

(v) *Amount per ton.* Robenidine hydrochloride, 30 grams (0.0033 percent) plus chlortetracycline, 500 grams.

(a) *Indications for use.* As an aid in the prevention of coccidiosis caused by *E. mivati*, *E. brunetti*, *E. tenella*, *E. acervulina*, *E. maxima*, and *E. necatrix*; as an aid in the reduction of mortality due to *E. coli* susceptible to chlortetracycline.

(b) *Limitations.* Withdraw 5 days prior to slaughter; do not feed to layers; not to be fed continuously for more than 5 days; as chlortetracycline hydrochloride provided by sponsor No. 010042, § 510.600(c) of this chapter.

(vi) *Amount per ton.* Robenidine hydrochloride, 30 grams (.0033 percent) plus bacitracin, 4 to 50 grams (as zinc bacitracin).

(a) *Indications for use.* As an aid in the prevention of coccidiosis caused by *E. mivati*, *E. brunetti*, *E. tenella*, *E. acervulina*, *E. maxima*, and *E. necatrix*; and in the presence of 4 to 30 grams per ton of bacitracin, for increased rate of weight gain; in the presence of 27 to 50 grams per ton of bacitracin, for improved feed efficiency.

(b) *Limitations.* Feed continuously as sole ration; do not feed to laying chickens; withdraw 5 days prior to slaughter; as zinc bacitracin provided by No. 011716 in § 510.600(c) of this chapter.

(vii) *Amount per ton.* Robenidine hydrochloride, 30 grams (.0033 percent) plus bacitracin, 4 to 50 grams (as bacitracin methylene disalicylate).

(a) *Indications for use.* As an aid in the prevention of coccidiosis caused by *E. mivati*, *E. brunetti*, *E. tenella*, *E. acervulina*, *E. maxima*, and *E. necatrix*; and in the presence of 4 to 30 grams per ton of bacitracin, for increased rate of weight gain; in the presence of 27 to 50 grams per ton of bacitracin, for improved feed efficiency.

(b) *Limitations.* Feed continuously as sole ration; do not feed to laying chickens; withdraw 5 days prior to slaughter; as bacitracin methylene disalicylate provided by No. 046573 in § 510.600(c) of this chapter.

(viii) *Amount per ton.* Robenidine hydrochloride, 30 grams (0.0033 percent) plus lincomycin, 2 grams.

(a) *Indications for use.* For increase in rate of weight gain and improved feed efficiency and as an aid in prevention of coccidiosis caused by *E. mivati*, *E. brunetti*, *E. tenella*, *E. acervulina*, *E. maxima*, and *E. necatrix*.

(b) *Limitations.* Do not feed to laying hens; feed continuously as the sole ration; withdraw 5 days before slaughter; lincomycin as provided by No. 000009, § 510.600(c) of this chapter; approval for this combination granted to No. 000009 as identified in § 510.600(c) of this chapter.

(2) *For broiler chickens—(i) Amount.* 30 mg. Robenidine hydrochloride, 30 mg. (0.0033 percent) plus oxytetracycline, 200 mg.

(ii) *Indications for use.* As an aid in the prevention of coccidiosis caused by *Meria mivati*, *E. Brunetti*, *E. tenella*, *E. acervulina*, *E. maxima*, and *E. necatrix*; for the control of complicated chronic respiratory disease (CRD or sac infection) caused by *Mycoplasma gallisepticum* and *Escherichia coli*.

(iii) *Limitations.* Do not feed to laying chickens; feed continuously as the sole ration; withdraw 5 days before slaughter; do not use in feeds containing bentonite; feed must be used within 50 days of date of manufacture; tetracycline as provided by No. 0000 of this chapter.

FR 13959, Mar. 27, 1975, as amended at FR 23444, Aug. 8, 1975; 40 FR 39859, Aug. 1975; 41 FR 1062, Jan. 6, 1976; 41 FR 4, July 12, 1976; 41 FR 53002, Dec. 3, 1976; 51 FR 7400, Mar. 3, 1986; 52 FR 2686, 1987; 53 FR 20843, June 7, 1988]

525 Ronnel.

(a) *Approvals.* Type A medicated animal feed: (1) [Reserved]

(2) 5.5 percent in mineral mix to 50 in § 510.600(c) of this chapter.

(b) *Special considerations.* (1) Maximum level permitted in a Type B feed is 5.5 percent.

The label shall bear adequate directions and warnings for use, which also include:

(i) A statement in the case of Type B feed containing ronnel that such feed shall be thoroughly mixed with ground grain for top dressing with complete ration.

(ii) A statement that ronnel-Type B feed is to be used as the sole source of ronnel medication.

(iii) "Warning—Ronnel is a cholinesterase inhibitor. Do not use this product in animals simultaneously or within a few days before or after exposure to cholinesterase inhibiting drugs, pesticides, or chemicals."

(c) *Related tolerances.* See 40 CFR 180.177.

(d) *Conditions of use.* It is used in the feed of beef cattle and nonlactating dairy animals as follows:

(1) *Amount.* 0.00078 lb. (0.35 gram) per 100 lb. body weight per day for 14 days.

(i) *Indications for use.* Control of grubs.

(ii) *Limitations.* Feed 0.00078 lb. (0.35 gram) per 100 lb. of animal weight per day for 14 days in a Type B feed containing not over 0.26 percent ronnel; withdraw from dairy animals 10 days before calving; if dairy cows or heifers freshen during medication, or if medication has not been withdrawn the required 10 days prior to freshening, milk must not be used for food for 10 days after the last treatment; withdraw 10 days prior to slaughter.

(2) *Amount.* 0.0018 lb. (0.82 gram) per 100 lb. body weight per day for 7 days.

(i) *Indications for use.* Control of grubs; aid in the reduction of cattle lice, when the drug is used for cattle grub control.

(ii) *Limitations.* Feed 0.0018 lb. (0.82 gram) per 100 lb. animal weight per day for 7 days in a Type B feed containing not over 6 percent ronnel; withdraw from dairy animals 10 days before calving; if dairy cows or heifers freshen during medication, or if medication has not been withdrawn the required 10 days prior to freshening, milk must not be used for food for 10 days after the last treatment; withdraw 10 days prior to slaughter.

(3) *Amount.* 0.01375 lb. (6.24 gram) per 100 lb. body weight per month for not less than 75 days.

(i) *Indications for use.* Control of grubs and hornflies.

(ii) *Limitations.* Feed 0.25 lb. of a mineral Type B feed in granular form containing 5.5 percent ronnel per 100 lb. of animal weight per month for not

less than 75 days; withdraw from dairy animals 10 days before calving; if dairy cows or heifers freshen during medication, or if medication has not been withdrawn the required 10 days prior to freshening, milk must not be used for food for 10 days after the last treatment; withdraw 10 days prior to slaughter.

(4) *Amount.* 0.0009 lb. (0.41 gram) per 100 lb. body weight per day for 14 days.

(i) *Indications for use.* Control of grubs.

(ii) *Limitations.* Feed 0.0009 lb. (0.41 gm.) per 100 lb. of animal weight per day for 14 days in a Type B feed containing 0.3 percent ronnel; withdraw from dairy animals 10 days before calving, if dairy cows or heifers freshen during medication, or if medication has not been withdrawn the required 10 days prior to freshening, milk must not be used for food for 10 days after the last treatment; withdraw 10 days prior to slaughter.

(5) *Amount.* 0.012 lb. (5.5 gram) per 100 lb. body weight per month for not less than 75 days.

(i) *Indications for use.* Control of grubs and hornflies.

(ii) *Limitations.* Feed 0.2 lb. of mineral Type B feed containing 6 percent ronnel per 100 lb. of animal weight per month for not less than 75 days; withdraw from dairy animals 10 days before calving; if dairy cows or heifers freshen during medication, or if medication has not been withdrawn the required 10 days prior to freshening, milk must not be used for food for 10 days after the last treatments.

[40 FR 13959, Mar. 27, 1975, as amended at 40 FR 24722, June 10, 1975; 51 FR 7400, Mar. 3, 1986; 52 FR 2686, Jan. 26, 1987; 52 FR 12521, Apr. 17, 1987]

§ 558.530 Roxarsone.

(a) *Approvals.* Type A medicated articles: (1) 10, 20, and 50 percent to 011526 in § 510.600(c) of this chapter for use in making chicken and turkey feeds.

(2) 10, 20, 50, and 80 percent to 017210 in § 510.600(c) of this chapter for use in making chicken, turkey, and swine feeds.

(b) *Related tolerances.* See § 556.60 of this chapter.

(c) *NAS/NRC status.* The conditions of use are NAS/NRC reviewed and found effective. NADA's for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety information.

(d) *Conditions of use—(1) Growing chickens and growing turkeys—(i) Grams per ton.* Roxarsone 22.7 and 45.4 (0.0025 to 0.005 percent).

(ii) *Indications for use.* For increased rate of weight gain, improved feed efficiency, and improved pigmentation.

(iii) *Limitations.* Withdraw 5 days before slaughter; as sole source of organic arsenic; drug overdose or lack of water may result in leg weakness; feed continuously throughout growing period.

(2) *Growing-finishing swine—(i) Grams per ton.* Roxarsone 22.7 to 34.1 (0.0025 to 0.00375 percent).

(a) *Indications for use.* For increased rate of weight gain and improved feed efficiency.

(b) *Limitations.* Withdraw 5 days before slaughter; as sole source of organic arsenic; feed continuously throughout growing season.

(ii) *Grams per ton.* Roxarsone 181.5 (0.02 percent).

(a) *Indications for use.* For the treatment of swine dysentery.

(b) *Limitations.* Feed for not more than 6 consecutive days; if improvement is not observed, consult a veterinarian; withdraw 5 days before slaughter; as a sole source of organic arsenic; animals must consume enough medicated feed to provide a therapeutic dose.

(3) *Permitted combinations.* It may be used in accordance with this section in combination as follows:

(i) Aklomide as in § 558.35.

(ii) Amprolium as in § 558.55.

(iii) Amprolium and ethopabate as in § 558.58.

(iv) Bacitracin methylene disalicylate as in § 558.76.

(v) Bacitracin zinc as in § 558.78.

(vi) Bambermycins and bambermycins plus certain anticoccidials as in § 558.95.

(vii) Buquinolate as in § 558.105.

(viii) Chlortetracycline as in § 558.128.

- (ix) Clopidol as in § 558.175.
- (x) Decoquinat as in § 558.195.
- (xi) Monensin as in § 558.355.
- (xii) Nequinat as in § 558.365.
- (xiii) Nicarbazin as in § 558.366.
- (xiv) Nitromide and sulfanitran as in § 558.376.
- (xv) Robenidine hydrochloride as in § 558.515.
- (xvi) Sulfadimethoxine, ormetoprim as in § 558.575.
- (xvii) Zoalene as in § 558.680.
- (xviii) Penicillin and zoalene as in § 558.680.
- (ix) Lasalocid as in § 558.311.
- (x) Lasalocid sodium and lincomycin as in § 558.311.
- (xi) Monensin and virginiamycin as in § 558.355.
- (xii) Monensin and bacitracin zinc as in § 558.355.
- (c) Additional combinations. (i) Roxarsone may be used in combination "as an aid in the reduction of lesions due to *E. tenella*" as follows:
 - (i) Lasalocid as in § 558.311.
 - (ii) Lasalocid plus bacitracin methylenedisalicylate as in § 558.311.
 - (iii) Lasalocid plus lincomycin as in § 558.311.
 - (iv) Lasalocid and bacitracin zinc as in § 558.311.
- (d) Roxarsone may be used in combination with salinomycin as in § 558.550.
- (e) Roxarsone may be used in combination with salinomycin and bacitracin methylene disalicylate as in § 558.550.
- (f) Roxarsone may be used in combination with salinomycin and bacitracin as in § 558.550.
- (g) Roxarsone may be used in combination with halofuginone hydrobromide and bacitracin methylene disalicylate as in § 558.265.
- (h) Roxarsone may be used in combination with narasin as in § 558.363 of part.

§ 52331, Oct. 27, 1981, as amended at 14151, Apr. 2, 1982; 47 FR 33494, Aug. 26, 1982; 48 FR 38815, Aug. 26, 1983; 48 FR 10111, 1983; 49 FR 26716, June 29, 1984; 49 FR 30927, Aug. 2, 1984; 51 FR 7400, Feb. 2, 1986; 51 FR 29463, Aug. 18, 1986; 51 FR 10111, Dec. 8, 1986; 52 FR 2686, Jan. 26, 1987; 53 FR 10118, Jan. 15, 1988; 53 FR 24260, May 15, 1988.

§ 558.550 Salinomycin.

(a) *Approval.* Type A medicated articles: 30 grams of activity from salinomycin sodium biomass to 000031 in § 510.600(c) of this chapter.

(b) *Conditions of use.* (1) Broilers: It is used as follows:

(i)(a) *Amount per ton.* Salinomycin 40 to 60 grams.

(b) *Indications for use.* For the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*.

(c) *Limitations.* Feed continuously as sole ration. Do not feed to layers. Not approved for use with pellet binders. May be fatal if accidentally fed to adult turkeys or horses.

(ii)(a) *Amount per ton.* Salinomycin 40 to 60 grams and roxarsone 45 grams.

(b) *Indications for use.* For the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*, including some field strains of *E. tenella* which are more susceptible to roxarsone combined with salinomycin than to salinomycin alone.

(c) *Limitations.* Feed continuously as sole ration. Use as sole source of organic arsenic. Not approved for use with pellet binders. Do not feed to layers. May be fatal if accidentally fed to adult turkeys or horses. Withdraw 5 days before slaughter. Roxarsone as provided by No. 011801 or 017210 in § 510.600(c) of this chapter.

(iii)(a) *Amount per ton.* Salinomycin 40 to 60 grams and bacitracin methylenedisalicylate 4 to 30 grams.

(b) *Indications for use.* For the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati* for increased rate of weight gain and improved feed efficiency.

(c) *Limitation.* Feed continuously as sole ration. Not approved for use with pellet binders. Do not feed to layers. May be fatal if accidentally fed to adult turkeys or horses. Bacitracin methylenedisalicylate as provided by No. 046573 in § 510.600(c) of this chapter.

(iv)(a) *Amount per ton.* Salinomycin 40 to 60 grams with roxarsone 45.4

grams and bacitracin methylene disalicylate 4 to 50 grams.

(b) *Indications for use.* For the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*, including some field strains of *E. tenella* which are more susceptible to roxarsone combined with salinomycin than to salinomycin alone; for increased rate of weight gain.

(c) *Limitations.* Feed continuously as sole ration. Use as sole source of organic arsenic. Not approved for use with pellet binders. Do not feed to layers. May be fatal if accidentally fed to adult turkeys or horses. Withdraw 5 days before slaughter. Roxarsone as provided by No. 017210 and bacitracin as provided by No. 046573 in § 510.600(c) of this chapter.

(v)(a) *Amount per ton.* Salinomycin 40 to 60 grams per ton with roxarsone 22.7 to 45.4 grams per ton.

(b) *Indications for use.* For the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima* and for improved feed efficiency.

(c) *Limitations.* Feed continuously as sole ration. Use as sole source of organic arsenic. Not approved for use with pellet binders. Do not feed to layers. May be fatal if accidentally fed to adult turkeys or to horses. Withdraw 5 days before slaughter. Roxarsone as provided by No. 017210 in § 510.600(c) of this chapter.

(vi)(a) *Amount per ton.* Salinomycin 40 to 60 grams and bacitracin methylene disalicylate 4 to 50 grams.

(b) *Indications for use.* For the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*, and for improved feed efficiency.

(c) *Limitations.* Feed continuously as sole ration. Not approved for use with pellet binders. Do not feed to layers. May be fatal if accidentally fed to adult turkeys or horses. Bacitracin MD as provided by No. 046573 in § 510.600(c) of this chapter.

(vii)(a) *Amount per ton.* Salinomycin 40 to 60 grams and bacitracin zinc 10 to 50 grams.

(b) *Indications for use.* For the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*, and for increased rate of weight gain.

(c) *Limitations.* Feed continuously as sole ration. Not approved for use with pellet binders. Do not feed to layers. May be fatal if accidentally fed to adult turkeys or horses. Bacitracin zinc as provided by No. 011716 in § 510.600(c) of this chapter.

(viii)(a) *Amount per ton.* Salinomycin 40 to 60 grams with roxarsone 45.4 grams and bacitracin zinc 4 to 50 grams.

(b) *Indications for use.* For the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*, including some field strains of *E. tenella* which are more susceptible to roxarsone combined with salinomycin than to salinomycin alone; for increased rate of weight gain and improved feed efficiency.

(c) *Limitations.* See paragraph (b)(1)(iv)(c) of this section.

(ix)(a) *Amount per ton.* Salinomycin 40 to 60 grams with roxarsone 34.1 grams and bacitracin zinc 10 to 50 grams.

(b) *Indications for use.* For the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*, and for increased rate of weight gain and improved feed efficiency.

(c) *Limitations.* Feed continuously as sole ration. Use as sole source of organic arsenic. Do not feed to layers. May be fatal if accidentally fed to adult turkeys or horses. Withdraw 5 days before slaughter. Roxarsone as provided by No. 017210 and bacitracin as provided by No. 011716 in § 510.600(c) of this chapter.

(x)(a) *Amount per ton.* Salinomycin 40 to 60 grams and virginiamycin 5 grams.

(b) *Indications for use.* For the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*, and for increased rate of weight gain and improved feed efficiency.

(c) *Limitations.* Feed continuously as sole ration. Not approved for use with pellet binders. Do not feed to layers or to chickens over 16 weeks of age. May be fatal if accidentally fed to adult turkeys or horses. Virginiamycin as provided by No. 000007 in § 510.600(c) of this chapter.

(xi)(a) *Amount per ton.* Salinomycin 40 to 60 grams and virginiamycin 5 to 15 grams.

(b) *Indications for use.* For the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*, and for increased rate of weight gain.

(c) *Limitations.* See paragraph (b)(1)(x)(c) of this section.

(xii) (a) *Amount per ton.* Salinomycin 40 to 60 grams, virginiamycin 5 grams, and roxarsone 45.4 grams.

(b) *Indications for use.* For prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*, including some field strains of *E. tenella* which are more susceptible to roxarsone combined with salinomycin than to roxarsone alone, and for improved feed efficiency.

(c) *Limitations.* Feed continuously as sole ration. Withdraw 5 days prior to slaughter. Use as sole source of organic arsenic. Not approved for use with pellet binders. Do not feed to layers. May be fatal if accidentally fed to adult turkeys or horses. Virginiamycin as provided by No. 000007 in § 510.600(c) of this chapter. Roxarsone as provided by No. 017210 in § 510.600(c) of this chapter.

(2) [Reserved]

(3) *Permitted combinations.* Salinomycin may be used as in this section in combinations as follows:

(i) Bambermycins and roxarsone as in § 558.95.

(ii) Bambermycins as in § 558.95.

[48 FR 30616, July 5, 1983]

EDITORIAL NOTE: For FEDERAL REGISTER citations affecting § 558.565, see the List of CFR Sections Affected in the Finding Aids section of this volume.

§ 558.565 Styrylpyridinium chloride, diethylcarbamazine.

(a) *Approvals.* To 000859 in § 510.600(c) of this chapter for a feed,

each pound containing a combination of either:

Styrylpyridinium chloride	Diethylcarbamazine (base)
(1) 0.035 percent (160 milligrams/pound).	0.021 percent (96 milligrams/pound).
(2) 0.039 percent (178 milligrams/pound).	0.024 percent (107 milligrams/pound).

(b) *Conditions of use in dogs*—(1) *Amount.* (i) 0.035 percent styrylpyridinium chloride and 0.021 percent diethylcarbamazine (as base), administered: to maximum stressed dogs, an amount of feed in ounces equal to the dog's body weight in pounds divided by 4; to medium stressed dogs, an amount divided by 4.5; to low stressed dogs, an amount divided by 5; to underweight dogs, 10 percent more than the amounts specified; to overweight dogs, 10 percent less than the amounts specified, adjustments every 7 days until the desired body weight is obtained.

(ii) 0.039 percent styrylpyridinium chloride and 0.024 percent diethylcarbamazine (as base) administered at 4.5 ounces (1 packet) per 20 pounds of body weight, daily (2.5 milligrams of styrylpyridinium chloride and 1.5 milligrams of diethylcarbamazine per pound of body weight).

(2) *Indications for use.* Control of hookworms (*Ancylostoma caninum*) and roundworms (*Toxocara canis*), and prevention of heartworm disease (*Dirofilaria immitis*).

(3) *Limitations.* Dogs with established heartworm infections should not be treated until converted to a negative status. For prevention of heartworm infestation, administer before the mosquito season and as soon as young puppies are born. Administer continuously during periods of exposure to hookworm, roundworm, and heartworm to control recurring burdens of hookworms and roundworms and prevent maturation of immature heartworms (third stage infective larvae) into adults. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

§ 558.575

[46 FR 43832, Sept. 1, 1981, as amended at 47 FR 14150, Apr. 2, 1982]

§ 558.575 Sulfadimethoxine, ormetoprim.

(a) *Approvals.* Type A medicated articles to sponsors as identified in § 510.600(c) of this chapter for uses as in paragraph (c) of this section as follows:

(1) 25 percent sulfadimethoxine and 15 percent ormetoprim to 000004 for use for poultry as in paragraphs (c)(1), (2), (3), and (4) of this section.

(2) 25 percent sulfadimethoxine and 5 percent ormetoprim to 000004 for use for fish as in paragraphs (c)(5) and (6) of this section.

(b) *Related tolerances.* See §§ 556.490 and 556.640 of this chapter.

(c) *Conditions of use.* It is used in feeds for animals as follows:

(1) *Broiler chickens—(i) Amount per ton.* Sulfadimethoxine, 113.5 grams (0.0125 percent) plus ormetoprim, 68.1 grams (0.0075 percent).

(a) *Indications for use.* As an aid in the prevention of coccidiosis caused by all *Eimeria* species known to be pathogenic to chickens, namely, *E. tenella*, *E. necatrix*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*, and bacterial infections due to *H. gallinarum* (infectious coryza), *E. coli* (colibacillosis) and *P. multocida* (fowl cholera).

(b) *Limitations.* Feed as sole ration; withdraw 5 days before slaughter.

(ii) *Amount per ton.* Sulfadimethoxine, 113.5 grams (0.0125 percent) plus ormetoprim, 68.1 grams (0.0075 percent) plus roxarsone, 22.7 grams (0.0025 percent).

(a) *Indications for use.* As an aid in the prevention of coccidiosis caused by all *Eimeria* species known to be pathogenic to chickens, namely *E. tenella*, *E. necatrix*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*, and bacterial infections due to *H. gallinarum* (infectious coryza), *E. coli* (colibacillosis); and *P. multocida* (fowl cholera); growth promotion and feed efficiency; improving pigmentation.

(b) *Limitations.* Withdraw 5 days before slaughter; as sole source of organic arsenic.

(2) *Replacement chickens—(i) Amount per ton.* Sulfadimethoxine, 113.5 grams (0.0125 percent) plus ormetoprim, 68.1 grams (0.0075 percent).

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(ii) *Indications for use.* As an aid in the prevention of coccidiosis caused by all *Eimeria* species known to be pathogenic to chickens, namely *E. tenella*, *E. necatrix*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*, and bacterial infections due to *H. gallinarum* (infectious coryza), *E. coli* (colibacillosis) and *P. multocida* (fowl cholera).

(iii) *Limitations.* Feed as a sole ration; do not feed to chickens over 16 weeks (112 days) of age; withdraw 5 days before slaughter.

(3) *Turkeys—(i) Amount per ton.* Sulfadimethoxine, 56.75 grams (0.00625 percent) plus ormetoprim, 34.05 grams (0.00375 percent).

(ii) *Indications for use.* As an aid in the prevention of coccidiosis caused by all *Eimeria* species known to be pathogenic to turkeys, namely, *E. adenoeides*, *E. gallopavonis*, and *E. meleagris* and bacterial infection due to *P. multocida* (fowl cholera).

(iii) *Limitations.* Do not feed to turkeys producing eggs for food; withdraw 5 days before slaughter.

(4) *Ducks—(i) Amount per ton.* Sulfadimethoxine, 227 grams (0.025 percent) plus ormetoprim, 136.2 grams (0.015 percent).

(a) *Indications for use.* As an aid in the control of bacterial infections due to *P. multocida* (fowl cholera) in ducks, including breeding ducks.

(b) *Limitations.* Feed as sole ration for 7 days; withdraw 5 days before slaughter; medication should be started at the first signs of infection; do not feed to ducks producing eggs for food.

(ii) *Amount per ton.* Sulfadimethoxine, 454 grams (0.05 percent) plus ormetoprim, 272.4 grams (0.03 percent).

(a) *Indications for use.* As an aid in the control of bacterial infections due to *E. coli*, *P. anatispestifer*, and severe challenge of *P. multocida* (fowl cholera) in ducks.

(b) *Limitations.* Feed as a sole ration for 7 days; withdraw 5 days before slaughter; medication should be started at the first signs of infection; not for breeding ducks; do not feed to ducks producing eggs for food.

(5) *Salmonids*—(i) *Amount*. 50 milligrams of active ingredients per kilogram of body weight per day.

(ii) *Indications for use*. For the control of furunculosis in salmonids (trout and salmon) caused by *Aeromonas salmonicida* strains susceptible to sulfadimethoxine and ormetoprim combination.

(iii) *Limitations*. Administer for 5 consecutive days; withdraw 42 days before release as stocker fish or slaughter.

(6) *Catfish*—(i) *Amount*. 50 milligrams of active ingredients per kilogram of body weight per day.

(ii) *Indications for use*. For control of enteric septicemia of catfish caused by *Edwardsiella ictaluri* strains susceptible to sulfadimethoxine and ormetoprim combination.

(iii) *Limitations*. Administer for 5 consecutive days; withdraw 3 days before slaughter or release as stocker fish.

[40 FR 13959, Mar. 27, 1975, as amended at 42 FR 13550, Mar. 11, 1977; 49 FR 33442, Aug. 23, 1984; 49 FR 46371, Nov. 26, 1984; 51 FR 7400, Mar. 3, 1986; 51 FR 18884, May 23, 1986; 52 FR 2686, Jan. 26, 1987; 54 FR 1686, Jan. 17, 1989]

§ 558.579 Sulfathoxypyridazine.

(a) *Approvals*. Type A medicated articles: 5.5 percent for swine, and 5.5 and 11 percent for cattle to 010042 in § 510.600(c) of this chapter.

(b) *Related tolerances*. See § 556.650 of this chapter.

(c) *Conditions of use*. It is used in animal feed as follows:

(1) *Swine*—(i) *Amount*. 25 milligrams per pound body weight per day.

(ii) *Indications for use*. For treatment of bacterial scours, pneumonia, enteritis, bronchitis, septicemia accompanying *Salmonella choleraesuis* infection.

(iii) *Limitations*. Administer 1,000 grams per ton (0.11 percent) for not less than 4 days nor more than 10 days; do not treat within 10 days of slaughter; as sole source of sulfonamide; for use by or on the order of a licensed veterinarian.

(2) *Cattle*—(i) *Amount*. 25 milligrams per pound body weight per day.

(ii) *Indications for use*. For treatment of respiratory infections (pneu-

monia, shipping fever), foot rot, calf scours; as adjunctive therapy in septicemia accompanying mastitis and metritis.

(iii) *Limitations*. Administer as a top dressing or in mixed feed for 4 days; do not treat within 16 days of slaughter; as sole source of sulfonamide; milk that has been taken from animals during treatment and for 72 hours (6 milkings) after the latest treatment must not be used for food; for use by or on the order of a licensed veterinarian.

[41 FR 11005, Mar. 15, 1976, as amended at 51 FR 7400, Mar. 3, 1986; 52 FR 2686, Jan. 26, 1987]

§ 558.582 Sulfamerazine.

(a) *Approvals*. Type A medicated articles: 99 percent to 010042 in § 510.600(c) of this chapter.

(b) *Related tolerances*. See § 556.660 of this chapter.

(c) *Conditions of use*. It is used in fish feed for rainbow trout, brook trout, and brown trout as follows:

(1) *Amount*. 10 grams of sulfamerazine per 100 pounds of fish per day.

(2) *Indications for use*. Control of furunculosis.

(3) *Limitations*. Treat for not more than 14 days; do not treat within 3 weeks of marketing or stocking in stream open to fishing.

[41 FR 11005, Mar. 15, 1976, as amended at 51 FR 7400, Mar. 3, 1986]

§ 558.586 Sulfaminoxoline.

(a) *Approvals*. Type A medicated articles: 40 percent to 000006 in § 510.600(c) of this chapter.

(b) [Reserved]

(c) [Reserved]

(d) *NAS/NRC status*. The conditions of use specified in this section have been reviewed by NAS/NRC and are found effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency information. Applications must be accompanied by a written commitment to undertake the human safety studies required by FDA.

(e) *Special considerations*. (1) For control of outbreaks of disease, medication should be initiated as soon as

the diagnosis is determined. Medicated chickens, turkeys, and rabbits must actually consume enough medicated feed which provides a recommended dose of approximately 3.5 to 60 milligrams per pound per day in chickens, 2.5 to 100 milligrams per pound per day in turkeys, and 2.8 to 68 milligrams per pound per day in rabbits depending upon age and class of animal, ambient temperature, and other factors. Consult a veterinarian or poultry pathologist for diagnosis.

(2) [Reserved]

(f) *Conditions of use.* It is used as follows:

(1) *Chickens*—(i) *Amount.* 0.015 percent.

(a) *Indications for use.* As an aid in preventing outbreaks of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, and *E. brunetti* under average conditions of exposure.

(b) *Limitations.* Feed continuously from the time birds are placed on litter and continue past the age when coccidiosis is ordinarily a hazard. If death losses exceed 0.5 percent in a 2-day period, obtain a laboratory diagnosis. If coccidiosis is the cause, use the sulfaquinoxaline levels recommended for control of outbreaks, returning to the original dosage schedule after the outbreak has subsided. Losses may result from intercurrent disease, other conditions affecting drug intake, or variant strains of coccidia species which can contribute to the virulence of coccidiosis under field conditions. Do not treat chickens within 10 days of slaughter. Do not medicate chickens producing eggs for human consumption.

(ii) *Amount.* 0.0175 percent.

(a) *Indications for use.* As an aid in preventing outbreaks of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, and *E. brunetti* where excessive exposure to coccidia is increased due to overcrowding or other management factors.

(b) *Limitations.* Feed continuously from the time birds are placed on litter and continue past the age when coccidiosis is ordinarily a hazard. If death losses exceed 0.5 percent in a 2-day period, obtain a laboratory diagnosis. If coccidiosis is the cause, use the

sulfaquinoxaline levels recommended for control of outbreaks, returning to the original dosage schedule after the outbreak has subsided. Losses may result from intercurrent disease, other conditions affecting drug intake, or variant strains of coccidia species which can contribute to the virulence of coccidiosis under field conditions. Do not treat chickens within 10 days of slaughter. Do not medicate chickens producing eggs for human consumption.

(iii) *Amount.* 0.1 to 0.05 percent.

(a) *Indications for use.* As an aid in controlling outbreaks of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, and *E. brunetti*.

(b) *Limitations.* Feed at 0.1 percent level for first 48 to 72 hours. Skip 3 days; 0.05 percent for 2 days, skip 3 days; 0.05 percent for 2 days. If bloody droppings recur, give 0.05 percent for another 2 days. Do not treat chickens within 10 days of slaughter. Do not medicate chickens producing eggs for human consumption.

(2) *Turkeys*—(i) *Amount.* 0.0175 percent.

(a) *Indications for use.* As an aid in preventing outbreaks of coccidiosis caused by *Eimeria meleagritidis* and *E. adenocoides*.

(b) *Limitations.* Feed 0.0175 percent continuously during time birds are closely confined. May be continued for week to 10 days after flock is transferred to range to reduce danger of an outbreak following moving of the flock. Do not treat turkeys within 10 days of slaughter. Do not medicate turkeys producing eggs for human consumption.

(ii) *Amount.* 0.05 percent.

(a) *Indications for use.* As an aid in controlling outbreaks of coccidiosis caused by *Eimeria meleagritidis*, and *E. adenocoides*.

(b) *Limitations.* Feed 0.05 percent for 2 days. Follow with 3 days on regular feed and 2 more days on 0.05 percent sulfaquinoxaline feed. Again follow with 3 days on regular feed and 2 more days on 0.05 percent sulfaquinoxaline feed. Continue this schedule if necessary till all signs of the outbreaks have subsided. Do not treat turkeys within 10 days of slaughter. Do not

medicate turkeys producing eggs for human consumption.

(3) *Chickens and turkeys*—(i) Amount. 0.05 or 0.1 percent.

(a) *Indications for use.* As an aid in the control of acute fowl cholera caused by *Pasteurella multocida* susceptible to sulfaquinoxaline and fowl typhoid caused by *Salmonella gallinarum* susceptible to sulfaquinoxaline.

(b) *Limitations.* Feed 0.1 percent for 48 to 72 hours. Mortality should be brought under control. After medication, move birds to clean ground or to a clean house. If disease recurs, use 0.05 percent in feed again for 2 days. Do not treat chickens or turkeys within 10 days of slaughter for food. Do not medicate chickens or turkeys producing eggs for human consumption.

(ii) [Reserved]

(4) *Rabbits*—(i) Amount. 0.025 percent.

(a) *Indications for use.* As an aid in preventing coccidiosis caused by *Eimeria stiedae*.

(b) *Limitations.* Treatment to be started after weaning. Feed continuously for 30 days or feed medicated feed for 2 days out of every week until marketing. Do not treat within 10 days of slaughter.

(ii) Amount. 0.1 percent.

(a) *Indications for use.* As an aid in controlling outbreaks of coccidiosis caused by *Eimeria stiedae*.

(b) *Limitations.* Feed for 2 weeks. Do not treat within 10 days of slaughter.

[48 FR 3985, Jan. 28, 1983, as amended at 51 FR 7400, Mar. 3, 1986; 52 FR 2686, Jan. 26, 1987]

§ 558.600 Tiamulin.

(a) *Approvals.* Type A article containing 5, 10, or 113.4 grams of tiamulin (as tiamulin hydrogen fumarate) per pound to 054273 in § 510.600(c) of this chapter.

(b) *Related tolerances.* See § 556.738 of this chapter.

(c) *Conditions of use in swine*—(1) Amount. 35 grams of tiamulin per ton.

(i) *Indications for use.* For control of swine dysentery associated with *Treponema hyodysenteriae* susceptible to tiamulin.

(ii) *Limitations.* Feed continuously as sole ration on premises with a history of swine dysentery but where signs of disease have not yet occurred or following approved treatment of disease. Withdraw 2 days before slaughter. Not for use in swine over 250 pounds body weight. Use as only source of tiamulin. Swine being treated with tiamulin should not have access to feeds containing polyether ionophores (e.g., lasalocid, monensin, narasin, or salinomycin) as adverse reactions may occur.

(2) Amount. 10 grams of tiamulin per ton.

(i) *Indications for use.* For increased rate of weight gain and improved feed efficiency.

(ii) *Limitations.* Feed continuously as the sole ration. Not for use in swine weighing over 250 pounds. Use as sole source of tiamulin. Swine being treated with tiamulin should not have access to feeds containing polyether ionophores (e.g., lasalocid, monensin, narasin, or salinomycin) as adverse reactions may occur.

[52 FR 26956, July 17, 1987, as amended at 53 FR 39257, Oct. 6, 1988]

§ 558.615 Thiabendazole.

(a) *Approvals.* Dry Type A medicated articles: 22, 44.1, 66.1, and 88.2 percent to 000006 in § 510.600(c) of this chapter. The 66.1 percent Type A is solely for the manufacture of cane molasses liquid Type B feed which is mixed in dry feeds. The 88.2 percent Type A is used solely for the manufacture of an aqueous slurry for adding to a Type C dry cattle feed.

(b) *Special considerations.* Do not use in Type B or Type C medicated feed containing bentonite.

(c) *Related tolerances.* See § 556.730 of this chapter.

(d) *Conditions of use.* It is used in feed for animals as follows:

(1) *Cattle*—(i) Amount. 3 grams per 100 lb. body weight.

(a) *Indications for use.* Control of infections of gastrointestinal roundworms (*Trichostrongylus* spp., *Haemonchus* spp., *Ostertagia* spp., *Nematodirus* spp., *Oesophagostomum radiatum*).

(b) *Limitations.* Use 3 grams per 100 lb. body weight at a single dose; may

repeat once in 2 to 3 weeks; do not treat animals within 3 days of slaughter; milk taken from treated animals within 96 hours (8 milkings) after the latest treatment must not be used for food.

(ii) *Amount.* 5 grams per 100 lb. body weight.

(a) *Indications for use.* Control of severe infections of gastrointestinal roundworms (*Trichostrongylus* spp., *Haemonchus* spp., *Ostertagia* spp., *Nematodirus* spp., *Oesophagostomum radiatum*); control of infections of *Cooperia* spp.

(b) *Limitations.* 5 grams per 100 lb. body weight at a single dose or divided into 3 equal doses, administered 1 dose each day, on succeeding days; may repeat once in 2 to 3 weeks; do not treat animals within 3 days of slaughter; milk taken from treated animals within 96 hours (8 milkings) after the latest treatment must not be used for food.

(2) *Goats*—(i) *Amount.* 3 grams per 100 lb. body weight.

(ii) *Indications for use.* Control of severe infections of gastrointestinal roundworms (*Trichostrongylus* spp., *Haemonchus* spp., *Ostertagia* spp., *Cooperia* spp., *Nematodirus* spp., *Bunostomum* spp., *Strongyloides* spp., *Chabertia* spp., and *Oesophagostomum* spp.).

(iii) *Limitations.* 3 grams per 100 lb. body weight at a single dose; do not treat animals within 30 days of slaughter; milk taken from treated animals within 96 hours (8 milkings) after the latest treatment must not be used for food.

(3) *Sheep and goats*—(i) *Amount.* 2 grams per 100 lb. body weight.

(ii) *Indications for use.* Control of infections of gastrointestinal roundworms (*Trichostrongylus* spp., *Haemonchus* spp., *Ostertagia* spp., *Cooperia* spp., *Nematodirus* spp., *Bunostomum* spp., *Strongyloides* spp., *Chabertia* spp., and *Oesophagostomum* spp.); also active against ova and larvae passed by sheep from 3 hours to 3 days after the feed is consumed (good activity against ova and larvae of *T. colubriformis* and *axei*, *Ostertagia* spp., *Nematodirus* spp., *Strongyloides* spp.; less effective against those of

Haemonchus contortus and *Oesophagostomum* spp.).

(iii) *Limitations.* Use 2 grams per 100 lb. body weight at a single dose; do not treat animals within 30 days of slaughter; milk taken from treated animals within 96 hours (8 milkings) after the latest treatment must not be used for food.

(4) *For swine*—(i) *Amount.* 45.4-908 grams per ton (0.005-0.1 percent).

(ii) *Indications for use.* Aid in the prevention of infections of large roundworms (genus *Ascaris*).

(iii) *Limitations.* Administer continuously feed containing 0.05-0.1 percent thiabendazole per ton for 2 weeks followed by feed containing 0.005-0.02 percent thiabendazole per ton for 8-14 weeks; do not treat animals within 30 days of slaughter.

(5) *Pheasants*—(i) *Amount.* 454 grams per ton (0.05 percent) continuously for 2 weeks (14 days).

(ii) *Indications for use.* For the treatment of gapeworms (*Syngamus trachea*) in pheasants.

(iii) *Limitations.* Do not use treated pheasants for food for 21 days after last day of treatment. Fertility, hatchability, and other reproductive data are not available on use in breeding animals.

[40 FR 13959, Mar. 27, 1975, as amended at 47 FR 49641, Nov. 2, 1982; 49 FR 29958, July 25, 1984; 51 FR 7400, Mar. 3, 1986; 52 FR 2686, Jan. 26, 1987]

§ 558.625 Tylosin.

(a) *Specifications.* Tylosin is the antibiotic substance produced by growth of *Streptomyces fradiae* or the same antibiotic substance produced by any other means. Tylosin, present as the phosphate salt, conforms to the appropriate antibiotic standard. Tylosin contains at least 95 percent tylosin as a combination of tylosin A, tylosin B, tylosin C, and tylosin D of which at least 80 percent is tylosin A as determined by a method entitled "Determination of Factor Content in Tylosin by High Performance Liquid Chromatography," which is incorporated by reference. Copies are available from the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rock-

ville, MD 20857, or available for inspection at the Office of the Federal Register, 1100 L St. NW., Washington, DC 20408.

(b) *Approvals.* Type A medicated article levels of tylosin granted to firms as sponsor(s) and identified by drug listing numbers in § 510.600(c) of this chapter for the specific usage indicated in paragraph (f) of this section.

(1) To 000986: 10, 40, 100 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.

(2) To 051359: 1, 2, 4, 5, 8, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.

(3) To 043733: 4 grams per pound, paragraph (f)(1)(vi)(a) of this section; 5, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.

(4) To No. 011490: 4 and 8 grams per pound, paragraph (f)(1)(vi)(a) of this section; 5, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.

(5) To 017800: 0.4, 0.8, 1, and 8 grams per pound, paragraph (f)(1)(vi)(a) of this section; 10 and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.

(6)–(7) [Reserved]

(8) To 035369: 4 and 10 grams per pound, paragraph (f)(1)(vi)(a) of this section; 10 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.

(9) To 043727: 4 grams per pound, paragraph (f)(1)(vi)(a) of this section; 5, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.

(10) To 012286: 0.4, 0.8, and 1.6 grams per pound, paragraph (f)(1)(vi)(a) of this section; 40 and 100 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.

(11) To 017274: 4, 8, and 10 grams per pound, paragraph (f)(1)(vi)(a) of this section; 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.

(12) To 021930: 2 grams per pound, paragraph (f)(1)(vi)(a) of this section; 5, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.

(13) To 035393: 0.4 and 2 grams per pound; paragraph (f)(1)(vi)(a) of this section.

(14) To 016968: 1, 2, 4, 8, and 10 grams per pound, paragraphs (f)(1) (i), (iii), (iv), and (vi) of this section; 20, 25, 40, and 100 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.

(15) To 026186: 1.6, 4, 10, and 20 grams per pound, paragraph (f)(1)(vi)(a) of this section; 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.

(16) To 049768: 5, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.

(17) To 021780: 0.8 gram per pound, paragraph (f)(1)(vi)(a) of this section; 5, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.

(18) [Reserved]

(19) To 033999: 10 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.

(20) To 033071: 0.4, 0.8, and 1.6 grams per pound; paragraph (f)(1)(vi)(a) of this section.

(21) [Reserved]

(22) To 026282: 10 grams per pound; paragraph (f)(1)(vi)(a) of this section.

(23) To 030804: 2 and 0.8 grams per pound; paragraph (f)(1)(vi)(a) of this section.

(24) [Reserved]

(25) To 000007: 4, 8, and 10 grams per pound, paragraph (f)(1)(vi)(a) of this section; 20 and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.

(26) To 034418: 10 grams per pound; paragraph (f)(1)(vi)(a) of this section.

(27) To 020275: 8 grams per pound, paragraphs (f)(1) (i), (iii), (iv), and (vi) of this section; 5, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.

(28) To 034139: 0.8 gram and 4 grams per pound, paragraph (f)(1)(vi)(a) of this section; 10 grams per pound, paragraphs (f)(1) (i), (iii), (iv), and (vi) of this section; 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.

(29)–(30) [Reserved]

(31) To 029341: 5 grams per pound; paragraph (f)(1)(vi)(a) of this section.

- (32) To 018597: 0.4 gram per pound; paragraph (f)(1)(vi)(a) of this section.
- (33) To 034936: 0.8 and 2 grams per pound, paragraph (f)(1)(vi)(a) of this section; 4, 8, and 10 grams per pound, paragraphs (f)(1)(i), (iii), (iv), and (vi) of this section; 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section; 100 grams per pound, paragraphs (f)(1) (i), (ii), (iii), (iv), and (vi) of this section.
- (34) To 028260: 0.8 gram per pound, paragraph (f)(1)(vi)(a) of this section.
- (35) To 039741: 2 and 10 grams per pound, paragraph (f)(1)(vi)(a) of this section.
- (36)—(37) [Reserved]
- (38) To 011749: 1 gram per pound, paragraph (f)(1)(vi)(a) of this section; 5, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.
- (39) To 053617: 10 grams per pound, paragraph (f)(1)(vi)(a) of this section.
- (40) To 035955: 10 grams per pound, paragraph (f)(1)(vi)(a) of this section.
- (41) [Reserved]
- (42) To 010439: 0.4, 0.5, and 2 grams per pound, paragraph (f)(1)(vi) (a) of this section; 5, 10, 20, and 40 grams per pound, paragraph (f)(1)(i) through (vi) of this section.
- (43)—(44) [Reserved]
- (45) To 017139: 4 and 10 grams per pound, paragraph (f)(1)(vi)(a) of this section.
- (46) To 017475: 0.4, 0.8, and 10 grams per pound; paragraph (f)(1)(vi)(a) of this section.
- (47) To 039502: 10 grams per pound; paragraph (f)(1)(vi)(a) of this section.
- (48) To 017790: 5, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.
- (49) To 021533: 2 and 10 grams per pound; paragraph (f)(1)(vi)(a) of this section.
- (50) To No. 018083: 4 grams per pound, paragraph (f)(1)(vi)(a) of this section; 5, 8, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.
- (51) To 017519: 5, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.
- (52) To 021810: 5, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.
- (53) To 034500: 4 and 10 grams per pound; paragraph (f)(1)(vi)(a) of this section.
- (54) To 030841: 5, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.
- (55) [Reserved]
- (56) To 026848: 10 grams per pound, paragraph (f)(1)(vi)(a) of this section; 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.
- (57) To 028459: 0.4 and 10 grams per pound; paragraph (f)(1)(vi)(a) of this section.
- (58)—(59) [Reserved]
- (60) To 017476: 2 grams per pound; paragraph (f)(1)(vi)(a) of this section.
- (61)—(62) [Reserved]
- (63) To 046987: 5, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.
- (64) [Reserved]
- (65) To No. 022422: 10 grams per pound, paragraphs (f)(1) (i), (iii), (iv), and (vi) of this section; 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.
- (66) To 024174: 5, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.
- (67) To 027190: 2 grams per pound; paragraph (f)(1)(vi)(a) of this section.
- (68) To 017473: 10 and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.
- (69) To 026948: 5, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.
- (70) [Reserved]
- (71) To 050568: 4 grams per pound, paragraph (f)(1)(vi)(a) of this section; 5, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.
- (72) To 012190: 5, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.
- (73) To 035098: 0.33 and 0.67 gram per pound, paragraph (f)(1)(vi)(a) of this section; 0.8, 1, 2, and 10 grams per pound, paragraphs (f)(1) (i) and (vi) (a), (b) and (d) of this section; 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.
- (74) [Reserved]
- (75) To 035221: 1, 2, and 5 grams per pound; paragraph (f)(1)(vi)(a) of this section.

- (76) To 021502: 10 grams per pound; paragraph (f)(1)(vi)(a) of this section.
- (77) To 050639: 5, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.
- (78) To 050972: 0.36, 0.4, 0.72, and 0.8 gram per pound, paragraph (f)(1)(vi)(a) of this section; 1 gram per pound, paragraphs (f)(1)(vi) (a), (b), and (d) of this section.
- (79) To 047427: 5, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.
- (80) To 049685: 5, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.
- (81) [Reserved]
- (82) To 026439: 5, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.
- (83) To 021676: 5-, 10-, 20-, and 40-grams per pound, paragraphs (f)(1) (i) through (vi) of this section.
- (84) To 043734: 4, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.
- (85) To 047126: 10, 40, and 100 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.
- (86) To 047863: 5, 10, 20, and 40 grams per pound, paragraphs (f)(1) (i) through (vi) of this section.
- (87) To 048696: 5, 10, 20, and 40 grams per pound paragraph (f)(1) (i) through (vi) of this section.
- (88) To 023368: 5, 10, 20, and 40 grams per pound, paragraph (f)(1) (i) through (vi) of this section.
- (89) To 053389: 5, 10, 20, and 40 grams per pound, paragraph (f)(1) (i) through (vi) of this section.
- (c) [Reserved]
- (d) [Reserved]
- (e) *Related tolerances.* See § 556.740 of this chapter.
- (f) *Conditions of use.* (1) It is used in animal feeds as follows:
- (i) *For beef cattle—(a) Amount per ton.* 8-10 grams.
- (b) *Indications for use.* For reduction of incidence of liver abscesses caused by *Fusobacterium necrophorum* and *Corynebacterium pyogenes*.
- (c) *Limitations.* As tylosin phosphate; each animal must receive not more than 90 milligrams per day and not less than 60 milligrams per day; feed continuously as sole ration.
- (ii) *Broiler chickens—(a) Amount per ton.* Tylosin, 800-1000 grams.
- (b) *Indications for use.* To aid in the control of chronic respiratory disease caused by *Mycoplasma gallisepticum*.
- (c) *Limitations.* As tylosin phosphate; withdraw 5 days before slaughter; administer in feed to chickens 0 to 5 days of age, follow with second administration in feed for 24-48 hours at 3 to 5 weeks of age.
- (iii) *Chickens—(a) Amount per ton.* Tylosin, 4-50 grams.
- (1) *Indications for use.* For increased rate of weight gain and improved feed efficiency.
- (2) *Limitations.* As tylosin phosphate.
- (iv) *Laying chickens—(a) Amount per ton.* Tylosin, 20-50 grams.
- (b) *Indications for use.* For improved feed efficiency.
- (c) *Limitations.* As tylosin phosphate.
- (v) *Replacement chickens—(a) Amount per ton.* Tylosin, 1,000 grams.
- (b) *Indications for use.* To aid in the control of chronic respiratory disease caused by *Mycoplasma gallisepticum*.
- (c) *Limitations.* As tylosin phosphate; withdraw 5 days before slaughter; administer in feed to chickens 0 to 5 days of age, follow with second administration in feed for 24 to 48 hours at 3 to 5 weeks of age.
- (vi) *Swine—(a) Amount per ton.* Tylosin, 10-100 grams.
- (1) *Indications for use.* For increased rate of weight gain and improved feed efficiency.
- (2) *Limitations.* As tylosin phosphate; continuous use as follows: Grams per ton: 20-100, prestarter or starter; 20-40, grower; 10-20, finisher.
- (b) *Amount per ton.* Tylosin, 40-100 grams.
- (1) *Indications for use.* Prevention of swine dysentery (vibronic).
- (2) *Limitations.* Use 100 grams per ton for at least 3 weeks followed by 40 grams per ton until market weight; as tylosin phosphate.
- (c) *Amount per ton.* Tylosin, 40-100 grams.
- (1) *Indications for use.* Treatment and control of swine dysentery (vibronic).
- (2) *Limitations.* Administer in feed as tylosin phosphate after treatment

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with tylosin in drinking water as tylosin base; 0.25 gram per gallon in drinking water for 3-10 days, 40-100 grams per ton in feed for 2-6 weeks.

(d) *Amount per ton.* Tylosin, 100 grams.

(1) *Indications for use.* Maintaining weight gains and feed efficiency in presence of atrophic rhinitis.

(2) *Limitations.* As tylosin phosphate.

(2) Tylosin may be used in accordance with the provisions of this section in the combinations provided as follows:

(i) Hygromycin B as in § 558.274.

(ii)-(iii) [Reserved]

(iv) Monensin in accordance with § 558.355.

(v) Pyrantel tartrate in accordance with § 558.485.

[40 FR 13959, Mar. 27, 1975]

EDITORIAL NOTE: For FEDERAL REGISTER citations affecting § 558.625, see the List of CFR Sections Affected in the Finding Aids section of this volume.

§ 558.630 Tylosin and sulfamethazine.

(a) [Reserved]

(b) *Approvals.* Type A medicated article levels, a combination of equal amounts of tylosin and sulfamethazine, granted to firms as sponsor(s) and identified by drug listing numbers in § 510.600(c) of this chapter for the conditions of use indicated in paragraph (f) of this section.

(1) To 000986: 40 grams per pound each, paragraph (f)(2)(i).

(2) To 000986: 10 grams per pound each, paragraph (f)(2)(i).

(3) To 017274, 034500: 10 grams per pound each, paragraph (f)(2)(ii) of this section.

(4) To 021780: 2 grams per pound each, paragraph (f)(2)(ii) of this section.

(5) To 017800: 40 grams per pound each, paragraph (f)(2)(ii) of this section.

(6) To 017139: 4, 10, or 20 grams per pound each, paragraph (f)(2)(ii) of this section.

(7) To 021930: 2 grams per pound each, paragraph (f)(2)(i) of this section; 5, 10, 20, or 40 grams per pound each, paragraph (f)(2)(ii) of this section.

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(8) To 017274, 026186, 026848: 5 or 10 grams per pound each, paragraph (f)(2)(ii) of this section.

(9) To 022422: 5 grams per pound each, paragraph (f)(2)(ii) of this section.

(10) To 010439, 011490, 011740, 012190, 016968, 017274, 017473, 017519, 017790, 018083, 020275, 021676, 021780, 021810, 023368, 024174, 026948, 030841, 034139, 034936, 035098, 043727, 043733, 046987, 047427, 047863, 049685, 049768, 050568, 050639, and 051359 053389: 5, 10, 20, or 40 grams per pound each, paragraph (f)(2)(ii) of this section.

(c) [Reserved]

(d) [Reserved]

(e) *Related tolerances.* See §§ 556.670 and 556.740 of this chapter.

(f) *Conditions of use.* It is used in feed for swine as follows:

(1) *Amount per ton.* Tylosin, 100 grams plus sulfamethazine, 100 grams.

(2) *Indications for use.* (i) Maintaining weight gains and feed efficiency in the presence of atrophic rhinitis; lowering the incidence and severity of *Bordetella bronchiseptica* rhinitis; prevention of swine dysentery (vibronic); control of swine pneumonias caused by bacterial pathogens (*P. multocida* and/or *C. pyogenes*); for reducing the incidence of cervical lymphadenitis (jowl abscesses) caused by Group E Streptococci. Only the sulfamethazine portion of this combination is active in controlling jowl abscesses.

(ii) Maintaining weight gains and feed efficiency in the presence of atrophic rhinitis; lowering the incidence and severity of *Bordetella bronchiseptica* rhinitis; prevention of swine dysentery (vibronic); control of swine pneumonias caused by bacterial pathogens (*Pasteurella multocida* and/or *Corynebacterium pyogenes*).

(3) *Limitations.* As tylosin phosphate; withdraw 15 days before slaughter.

[40 FR 13959, Mar. 27, 1975]

EDITORIAL NOTE: For FEDERAL REGISTER citations affecting § 558.630, see the List of CFR Sections Affected in the Finding Aids section of this volume.

§ 558.635 Virginiamycin.

(a) [Reserved]

(b) *Approvals*. Type A medicated articles: (1) 1.1 percent activity (5 grams per pound), 2.2 percent activity (10 grams per pound), 4.4 percent activity (20 grams per pound), 11 percent activity (50 grams per pound), and 50 percent activity (227 grams per pound) to 000007 in § 510.600(c) of this chapter.

(2) 2.2 percent activity (10 grams per pound) to 011490, 016968, 017274, 017790, and 047427 in § 510.600(c) of this chapter for use as in paragraph (f)(1) (iv) and (v) of this section.

(c) [Reserved]

(d) *Related tolerances*. See § 556.750 of this chapter.

(e) *Special considerations*. (1) Not for use in breeding swine over 120 pounds.

(2) Dilute Type A article with at least 10 pounds of a feed ingredient prior to final mixing in 1 ton of Type C feed.

(f) *Conditions of use*—(1) *Swine*. It is used as follows:

(i) 100 grams per ton for 2 weeks, for treatment of swine dysentery in non-breeding swine over 120 pounds.

(ii) 100 grams per ton for 2 weeks, 50 grams per ton thereafter, for treatment and control of swine dysentery in swine up to 120 pounds.

(iii) 25 grams per ton, as an aid in control of dysentery in swine up to 120 pounds. For use in animals or on premises with a history of swine dysentery but where symptoms have not yet occurred.

(iv) 10 grams per ton from weaning up to 120 pounds for increased rate of weight gain and improved feed efficiency, followed by 5 grams per ton to market weight for increased rate of weight gain and improved feed efficiency. For continuous use from weaning to market weight.

(v) 10 grams per ton from weaning up to 120 pounds for increased rate of weight gain and improved feed efficiency, followed by 5 to 10 grams per

ton to market weight for increased rate of weight gain. For continuous use from weaning to market weight.

(2) *Poultry*. It is used as follows:

(i) 5 to 15 grams per ton for increased rate of weight gain, for use in broiler chickens, not for use in layers.

(ii) 5 grams per ton for increased rate of weight gain and improved feed efficiency in broiler chickens, not for use in layers.

(iii) 20 grams per ton for prevention of necrotic enteritis caused by *Clostridium perfringens* susceptible to virginiamycin in broiler chickens; not for use in layers.

(iv) 10 to 20 grams per ton for increased rate of weight gain and improved feed efficiency in growing turkeys.

(3) Virginiamycin may be used in accordance with the provisions of this section in the combinations provided, as follows:

(i) Monensin sodium in accordance with § 558.355.

(ii) Lasalocid sodium in accordance with § 558.311.

(iii) Monensin and roxarsone as in § 558.355.

(iv) Amprolium and ethopabate as in § 558.58.

(v) Halofuginone as in § 558.265.

(vi) Salinomycin alone or with roxarsone as in § 558.550.

[40 FR 13959, Mar. 27, 1975]

EDITORIAL NOTE: For FEDERAL REGISTER citations affecting § 558.635, see the List of CFR Sections Affected in the Finding Aids section of this volume.

§ 558.680 Zoalene.

(a) *Approvals*. Type A medicated articles: 25 percent to 017210 in § 510.600(c) of this chapter.

(b) *Related tolerances*. See § 556.770 of this chapter.

(c) *Conditions of use*—(1) *Chickens and turkeys*:

Zoalene in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
(i) 36.3 to 113.5 (0.004% to 0.0125%).		Replacement chickens; development of active immunity to coccidiosis.	Grower ration not to be fed to birds over 14 weeks of age; as follows—	
		Growing conditions	Starter ration	Grower ration
		Severe exposure	Grams per ton 113.5 (0.0125%)	Grams per ton 75.4-113.5 (0.008%–0.0125%)
		Light to moderate exposure	75.4-113.5 (0.0083%–0.0125%)	36.3-75.4 (0.004%–0.0087%)
		Arsanilate sodium 90 (0.01%).	Replacement chickens; development of active immunity to coccidiosis; growth promotion and feed efficiency; improving pigmentation.	Grower ration not to be fed to birds over 14 weeks of age; withdraw 5 d before slaughter; as sole source of organic arsenic; as follows—
		Growing conditions	Starter ration	Grower ration
		Severe exposure	Grams per ton 113.5 (0.0125%)	Grams per ton 75.4-113.5 (0.008%–0.0125%)
		Light to moderate exposure	75.4-113.5 (0.0083%–0.0125%)	36.3-75.4 (0.004%–0.0087%)
		Arsanilic acid 90 (0.01%).	Replacement chickens; development of active immunity to coccidiosis; growth promotion and feed efficiency; improving pigmentation.	Grower ration not to be fed to birds over 14 weeks of age; withdraw 5 d before slaughter; as sole source of organic arsenic; as follows—
		Growing conditions	Starter ration	Grower ration
		Severe exposure	Grams per ton 113.5 (0.0125%)	Grams per ton 75.4-113.5 (0.008%–0.0125%)
		Light to moderate exposure	75.4-113.5 (0.0083%–0.0125%)	36.3-75.4 (0.004%–0.0087%)
		Arsanilic acid 90 (0.01%) plus erythromycin 4.8 to 18.5.	Replacement chickens; growth promotion and feed efficiency; development of active immunity to coccidiosis; improving pigmentation.	As erythromycin thiocyanate; grower ration not to be fed to birds over 14 weeks of age; withdraw 5 d before slaughter; as sole source of organic arsenic; as follows—

Growing conditions	Starter ration	Grower ration
	Grams per ton	Grams per ton
Severe exposure.....	113.5 (0.0125%)	75.4-113.5 (0.0083%- 0.0125%)
Light to moderate exposure.....	75.4-113.5 (0.0083%- 0.0125%)	36.3-75.4 (0.004%- 0.0083%)

Arsanilic acid 90
(0.01%) plus
erythromycin 92.5.

1. Replacement chickens; as an aid in the prevention of chronic respiratory disease during periods of stress; development of active immunity to coccidiosis; growth promotion and feed efficiency; improving pigmentation.

Feed for 2 d before stress and 3 to 6 d after stress; as erythromycin thiocyanate; grower ration not to be fed to birds over 14 weeks of age; withdraw 5 d before slaughter; as sole source of organic arsenic; as follows—

Growing conditions	Starter ration	Grower ration
	Grams per ton	Grams per ton
Severe exposure.....	113.5 (0.0125%)	75.4-113.5 (0.0083%- 0.0125%)
Light to moderate exposure.....	75.4-113.5 (0.0083%- 0.0125%)	36.3-75.4 (0.004%- 0.0083%)

2. Replacement chickens; as an aid in the prevention of infectious coryza; development of active immunity to coccidiosis; growth promotion and feed efficiency; improving pigmentation.

Feed for 7 to 14 d; as erythromycin thiocyanate; grower ration not to be fed to birds over 14 weeks of age; withdraw 5 d before slaughter; as sole source of organic arsenic; as follows—

Growing conditions	Starter ration	Grower ration
	Grams per ton	Grams per ton
Severe exposure.....	113.5 (0.0125%)	75.4-113.5 (0.0083%- 0.0125%)
Light to moderate exposure.....	75.4-113.5 (0.0083%- 0.0125%)	36.3-75.4 (0.004%- 0.0083%)

Arsanilic acid 90
(0.01%) plus
erythromycin 185.

Replacement chickens; as an aid in the prevention and reduction of lesions and in lowering severity of chronic respiratory disease; growth promotion and feed efficiency; improving pigmentation and development of active immunity to coccidiosis.

Feed for 5 to 8 d; do not use in birds producing eggs for food purposes; withdraw 5 d before slaughter; as erythromycin thiocyanate; and as sole source of organic arsenic; as follows—

Growing conditions	Starter ration	Grower ration
	Grams per ton	Grams per ton
Severe exposure.....	113.5 (0.0125%)	75.4-113.5 (0.0083%- 0.0125%)

Growing conditions	Starter ration	Grower ration
Light to moderate exposure.....	75.4-113.5 (0.0083%-- 0.0125%)	38.3-75.4 (0.004%-- 0.0083%)

Arsanilic acid 90
(0.01%) plus
penicillin 2.4 to 50.

Replacement chickens; growth
promotion and feed efficien-
cy; development of active im-
munity to coccidiosis; improv-
ing pigmentation.

As procaine penicillin; grower
ration not to be fed to birds
over 14 weeks of age; with-
draw 5 d before slaughter; as
sole source of organic ar-
senic; as follows—

Growing conditions	Starter ration	Grower ration
	Grams per ton	Grams per ton
Severe exposure.....	113.5 (0.0125%)	75.4-113.5 (0.0083%-- 0.0125%)
Light to moderate exposure.....	75.4-113.5 (0.0083%-- 0.0125%)	38.3-75.4 (0.004%-- 0.0083%)

Bacitracin 100 to 500...

Replacement chickens; treat-
ment of chronic respiratory
disease (air-sac infection);
blue comb (nonspecific infec-
tious enteritis); development
of active immunity to coccid-
iosis.

As bacitracin zinc; grower
ration not to be fed to birds
over 14 weeks of age; as
follows—

Growing conditions	Starter ration	Grower ration
	Grams per ton	Grams per ton
Severe exposure.....	113.5 (0.0125%)	75.4-113.5 (0.0083%-- 0.0125%)
Light to moderate exposure.....	75.4-113.5 (0.0083%-- 0.0125%)	38.3-75.4 (0.004%-- 0.0083%)

Chlortetracycline 100
to 200.

Replacement chickens; treat-
ment of chronic respiratory
disease (air-sac infection);
blue comb (nonspecific infec-
tious enteritis); prevention of
synovitis; development of
active immunity to coccidiosis.

Not to be fed to laying chick-
ens; as chlortetracycline hy-
drochloride; grower ration not
to be fed to birds 14 weeks
of age; as follows—

Growing conditions	Starter ration	Grower ration
	Grams per ton	Grams per ton
Severe exposure.....	113.5 (0.0125%)	75.4-113.5 (0.0083%-- 0.0125%)
Light to moderate exposure.....	75.4-113.5 (0.0083%-- 0.0125%)	38.3-75.4 (0.004%-- 0.0083%)

Chlortetracycline 200 ... Replacement chickens; control of synovitis; development of active immunity to coccidiosis.

Not to be fed to laying chickens; as chlortetracycline hydrochloride; (grower ration not to be fed to birds over 14 weeks of age); as follows—

Growing conditions	Starter ration	Grower ration
	<i>Grams per ton</i>	<i>Grams per ton</i>
Severe exposure	113.5 (0.0125%)	75.4-113.5 (0.0083%— 0.0125%)
Light to moderate exposure	75.4-113.5 (0.0083%— 0.0125%)	36.3-75.4 (0.004%— 0.0083%)

Erythromycin 4.6 to 18.5 ... Replacement chickens; growth promotion and feed efficiency; development of active immunity to coccidiosis.

As erythromycin thiocyanate; grower ration not to be fed to birds over 14 weeks of age; as follows—

Growing conditions	Starter ration	Grower ration
	<i>Grams per ton</i>	<i>Grams per ton</i>
Severe exposure	113.5 (0.0125%)	75.4-113.5 (0.0083%— 0.0125%)
Light to moderate exposure	75.4-113.5 (0.0083%— 0.0125%)	36.3-75.4 (0.004%— 0.0083%)

Erythromycin 92.5 ... 1. Replacement chickens; as an aid in the prevention of chronic respiratory disease during periods of stress; development of active immunity to coccidiosis.

Feed for 2 d before stress and 3 to 6 d after stress; withdraw 24 h before slaughter; as erythromycin thiocyanate; grower ration not to be fed to birds over 14 weeks of age; as follows—

Growing conditions	Starter ration	Grower ration
	<i>Grams per ton</i>	<i>Grams per ton</i>
Severe exposure	113.5 (0.0125%)	75.4-113.5 (0.0083%— 0.0125%)
Light to moderate exposure	75.4-113.5 (0.0083%— 0.0125%)	36.3-75.4 (0.004%— 0.0083%)

2. Replacement chickens; as an aid in the prevention of infectious coryza; development of active immunity to coccidiosis.

Feed for 7 to 14 d; withdraw 24 h before slaughter; as erythromycin thiocyanate; grower ration not to be fed to birds over 14 weeks of age; as follows—

Growing condition:	Starter ration	Grower ration
	Grams per ton	Grams per ton
Severe exposure	113.5 (0.0125%)	75.4-113.5 (0.0083%- 0.0125%)
Light to moderate exposure	75.4-113.5 (0.0083%- 0.0125%)	36.3-75.4 (0.004%- 0.0083%)

Erythromycin 185. Replacement chickens; as an aid in the prevention and reduction of lesions and in lowering severity of chronic respiratory disease; development of active immunity to coccidiosis. Feed for 5 to 8 d; do not use in birds producing eggs for food purposes; withdraw 48 h before slaughter; grower ration not to be fed to birds over 14 weeks of age; as follows—

Growing conditions	Starter ration	Grower ration
	Grams per ton	Grams per ton
Severe exposure	113.5 (0.0125%)	75.4-113.5 (0.0083%- 0.0125%)
Light to moderate exposure	75.4-113.5 (0.0083%- 0.0125%)	36.3-75.4 (0.004%- 0.0083%)

Hygromycin B 8 to 12. Replacement chickens; development of active immunity to coccidiosis; control of infestation of large round worms (*Ascaris galli*), cecal worms (*Heterakis gallinae*), and capillary worms (*Capillaria oblongata*). Grower ration not to be fed to birds over 14 weeks of age; as follows—

Growing conditions	Starter ration	Grower ration
	Grams per ton	Grams per ton
Severe exposure	113.5 (0.0125%)	75.4-113.5 (0.0083%- 0.0125%)
Light to moderate exposure	75.4-113.5 (0.0083%- 0.0125%)	36.3-75.4 (0.004%- 0.0083%)

Penicillin 2.4 to 50. Replacement chickens; growth promotion and feed efficiency; development of active immunity to coccidiosis. As procaine penicillin; grower ration not to be fed to birds over 14 weeks of age; as follows—

Growing conditions	Starter ration	Grower ration
	Grams per ton	Grams per ton
Severe exposure	113.5 (0.0125%)	75.4-113.5 (0.0083%- 0.0125%)
Light to moderate exposure	75.4-113.5 (0.0083%- 0.0125%)	36.3-75.4 (0.004%- 0.0083%)

Penicillin 2.4 to 50 plus roxarsone 22.7 to 45.4 (0.0025% to 0.005%).

Replacement chickens; growth promotion and feed efficiency; development of active immunity to coccidiosis; improving pigmentation.

As procaine penicillin; grower ration not to be fed to birds over 14 weeks of age; withdraw 5 d before slaughter; as sole source of organic arsenic; as follows—

Growing conditions	Starter ration	Grower ration
	Grams per ton	Grams per ton
Severe exposure	113.5 (0.0125%)	75.4-113.5 (0.0083%-0.0125%)
Light to moderate exposure	75.4-113.5 (0.0083%-0.0125%)	36.3-75.4 (0.004%-0.0083%)

Roxarsone 22.7 to 45.4 (0.0025% to 0.005%).

Replacement chickens; development of active immunity to coccidiosis; growth promotion and feed efficiency; improving pigmentation.

Grower ration not to be fed to birds over 14 weeks of age; withdraw 5 d before slaughter; as sole source of organic arsenic; as follows—

Growing conditions	Starter ration	Grower ration
	Grams per ton	Grams per ton
Severe exposure	113.5 (0.0125%)	75.4-113.5 (0.0083%-0.0125%)
Light to moderate exposure	75.4-113.5 (0.0083%-0.0125%)	36.3-75.4 (0.004%-0.0083%)

arsenic in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
113.5 (0.0125%)		Broiler chickens; prevention and control of coccidiosis.		
	Arseniate sodium 90 (0.01%).	Broiler chickens; prevention and control of coccidiosis; growth promotion and feed efficiency; improving pigmentation.	Withdraw 5 days before slaughter; as sole source of organic arsenic.	
	Arsenic acid 90 (0.01%).	Broiler chickens; prevention and control of coccidiosis; growth promotion and feed efficiency; improving pigmentation.	Withdraw 5 d before slaughter; as sole source of organic arsenic.	
	Arsenic acid 90 (0.01%) plus erythromycin 4.6 to 18.5.	Broiler chickens; growth promotion and feed efficiency; prevention and control of coccidiosis; improving pigmentation.	As erythromycin thiocyanate; withdraw 5 d before slaughter; as sole source of organic arsenic.	
	Arsenic acid 90 (0.01%) plus erythromycin 92.5.	1. Broiler chickens; aid in the prevention of chronic respiratory disease during periods of stress; growth promotion and feed efficiency; improving pigmentation; control of coccidiosis. 2. Broiler chickens; prevention and control of coccidiosis; growth promotion and feed efficiency; improving pigmentation; aid in the prevention of infectious coryza.	do	
			do	

Zoalene in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
	Arsanilic acid 90 (0.01%) plus erythromycin 185.	Broiler chickens; as an aid in the prevention and reduction of lesions and in lowering severity of chronic respiratory disease; prevention and control of coccidiosis; growth promotion and feed efficiency; improving pigmentation.	Feed for 5 to 8 d; do not use in birds producing eggs for food purposes; as erythromycin thiocyanate; withdraw 5 d before slaughter; as sole source of organic arsenic.	
	Arsanilic acid 90 (0.01%) plus penicillin 2.4 to 50.	Broiler chickens; growth promotion and feed efficiency; prevention and control of coccidiosis; improving pigmentation.	As procaine penicillin; withdraw 5 d before slaughter; as sole source of organic arsenic.	
	Arsanilic acid 90 (0.01%) plus bacitracin 4 to 50.	Broiler chickens; prevention and control of coccidiosis; improving pigmentation; growth promotion and feed efficiency.	Withdraw 5 d before slaughter; as sole source of organic arsenic; as bacitracin methylene disalicylate.	
	Bacitracin 4 to 50.	Broiler chickens; growth promotion and feed efficiency; prevention and control of coccidiosis.	As bacitracin methylene disalicylate, or zinc bacitracin.	
	Bacitracin 4 to 50 plus roxarsone 22.7 to 45.4 (0.0025% to 0.005%).	Broiler chickens; growth promotion and feed efficiency; prevention and control of coccidiosis; improving pigmentation.	As bacitracin methylene disalicylate, or zinc bacitracin; withdraw 5 d before slaughter; as sole source of organic arsenic.	
	Bacitracin 100 to 500.	Broiler chickens; treatment of chronic respiratory disease (air-sac infection); blue comb (nonspecific infectious enteritis); prevention and control of coccidiosis.	As zinc bacitracin.	
	Chlortetracycline 100 to 200.	Broiler chickens; treatment of chronic respiratory disease (air-sac infection); blue comb (nonspecific infectious enteritis); prevention of synovitis; prevention and control of coccidiosis.	Not to be fed to laying chickens; as chlortetracycline hydrochloride.	
	Chlortetracycline 200.	Broiler chickens; prevention and control of coccidiosis; control of synovitis.	Not to be fed to laying chickens; as chlortetracycline hydrochloride.	
	Erythromycin 4.6 to 18.5.	Broiler chickens; growth promotion and feed efficiency; prevention and control of coccidiosis.	As erythromycin thiocyanate.	
	Erythromycin 92.5.	1. Broiler chickens; aid in the prevention of chronic respiratory disease during period of stress; prevention and control of coccidiosis. 2. Broiler chickens; as an aid in the prevention of infectious coryza; prevention and control of coccidiosis.	Feed for 2 d before stress and 3 to 6 d after stress; withdraw 24 h before slaughter; as erythromycin thiocyanate. Feed for 7 to 14 d; withdraw 24 h before slaughter; as erythromycin thiocyanate.	
	Erythromycin 185.	Broiler chickens; as an aid in the prevention and reduction of lesions and in lowering severity of chronic respiratory disease; prevention and control of coccidiosis.	Feed for 5 to 8 d; do not use in birds producing eggs for food purposes; withdraw 48 h before slaughter; as erythromycin thiocyanate.	
	Hygromycin B (8 to 12).	Broiler chickens; prevention and control of coccidiosis; control of infestation of large round worms (<i>Ascaris galli</i>), cecal worms (<i>Heterakis gallinae</i>), and capillary worms (<i>Capillaria obsignata</i>).		

Zoalene in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
(a) 113.5 to 170.3 (0.0125% to 0.01875%).	Lincomycin 2.....	Broiler chickens; increase in rate of weight gain; improved feed efficiency; as an aid in the prevention and control of coccidiosis.	Do not feed to laying chickens; to be fed as the sole ration; as lincomycin hydrochloride monohydrate provided by No. 000009, see § 510.600(c) of this chapter; zoalene provided by No. 025700, see § 510.600(c) of this chapter.	
	Penicillin 2.4 to 50.....	Broiler chickens; growth promotion and feed efficiency; prevention and control of coccidiosis.	As procaine penicillin.....	
	Penicillin 2.4 to 50 plus roxarsone 22.7 to 45.4 (0.0025% to 0.005%).	Broiler chickens; prevention and control of coccidiosis; growth promotion and feed efficiency; improving pigmentation.	Withdraw 5 d before slaughter; as sole source of organic arsenic; as procaine penicillin.	
	Roxarsone 22.7 to 45.4 (0.0025% to 0.005%).	Broiler chickens; prevention and control of coccidiosis; growth promotion and feed efficiency; improving pigmentation.	Withdraw 5 d before slaughter; as sole source of organic arsenic.	
	Arseniate sodium 90 (0.01%).	Turkeys; prevention and control of coccidiosis.	For turkeys grown for meat purposes only.	
	Arsenite acid 90 (0.01%).	Turkeys; growth promotion and feed efficiency; improving pigmentation.	For turkeys grown for meat purposes only; withdraw 5 d before slaughter; as sole source of organic arsenic.	
	Carbarsone (not U.S.P.) 277 to 340.5 (0.025% to 0.0375%).	Turkeys; prevention and control of coccidiosis; aid in the prevention of blackhead.	For turkeys grown for meat purposes only; feed continuously beginning 2 weeks before blackhead and coccidiosis are expected and continue as long as prevention of blackhead and prevention and control of coccidiosis is needed; withdraw 5 d before slaughter; as sole source of organic arsenic.	
	Roxarsone 22.7 to 45.4 (0.0025% to 0.005%).	Turkeys; growth promotion and feed efficiency; improving pigmentation.	Withdraw 5 d before slaughter; as sole source of organic arsenic.	

(2) Permitted combinations. It may be used in accordance with the provisions of this section in the combinations provided, as follows:

(i) Bambermycins in accordance with § 558.95.

(ii) Roxarsone in accordance with § 558.530.

41 FR 11005, Mar. 15, 1976, as amended at 42 FR 18618, Apr. 8, 1977; 42 FR 20817, Apr. 12, 1977; 42 FR 38995, July 19, 1977; 51 FR 401, Mar. 3, 1986; 52 FR 2686, Jan. 26, 1987.

PART 564—DEFINITIONS AND STANDARDS FOR ANIMAL FOOD

Subpart A—General Provisions

Sec.

564.3 Definitions and interpretations.

564.5 Procedure for establishing a food standard.

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Subpart B—Food Additives in Standardized Animal Feed

564.20 Food additives proposed for use in animal foods for which definitions and standards of identity are established.

AUTHORITY: Secs. 401, 701, 52 Stat. 1046, 1055 as amended; 21 U.S.C. 341, 371.

SOURCE: 41 FR 38641, Sept. 10, 1976, unless otherwise noted.

Subpart A—General Provisions

§ 564.3 Definitions and interpretations.

(a) The definitions and interpretations of terms contained in section 201 of the Federal Food, Drug, and Cosmetic Act shall be applicable also to such terms when used in regulations promulgated under the Act.

(b) If a regulation prescribing a definition and standard of identity for a food has been promulgated under section 401 of the Act and the name therein specified for the food is used in any other regulation under section 401 or any other provision of the Act, such name means the food which conforms to such definition and standard, except as otherwise specifically provided in such other regulation.

(c) No provision of any regulation prescribing a definition and standard of identity or standard of quality or fill of container under section 401 of the Act shall be construed as in any way affecting the concurrent applicability of the general provisions of the Act and the regulations thereunder relating to adulteration and misbranding. For example, all regulations under section 401 of the Act contemplate that the food and all articles used as components or ingredients thereof shall not be poisonous or deleterious and shall be clean, sound, and fit for food. A provision in such regulations for the use of coloring or flavoring does not authorize such use under circumstances or in a manner whereby damage or inferiority is concealed or whereby the food is made to appear better or of greater value than it is.

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(d) "Safe and suitable" means that the ingredient:

(1) Performs an appropriate function in the food in which it is used.

(2) Is used at a level no higher than necessary to achieve its intended purpose in that food.

(3) Is not a food additive or color additive as defined in section 201 (s) or (t) of the Act as used in that food, or is a food additive or color additive as so defined and is used in conformity with regulations established pursuant to section 409 or 706 of the Act.

§ 564.5 Procedure for establishing a food standard.

(a) The procedure for establishing a food standard under section 401 of the Act shall be governed by Part 10 of this chapter.

(b) Any petition for a food standard shall show that the proposal, if adopted, would promote honesty and fair dealing in the interest of consumers.

(c) Any petition for a food standard shall assert that the petitioner commits himself to substantiate the information in the petition by evidence in a public hearing, if such a hearing becomes necessary.

(d) If a petitioner fails to appear, or to substantiate the information in his petition, at a public hearing on the matter, the Commissioner may either (1) withdraw the regulation and terminate the proceeding or (2) if he concludes that it is in accordance with the requirements of section 401 of the Act, continue the proceeding and introduce evidence to substantiate such information.

[42 FR 4717, Jan. 25, 1977, as amended at 42 FR 15675, Mar. 22, 1977]

§ 564.6 Review of Codex Alimentarius Food Standards.

(a) All food standards adopted by the Codex Alimentarius Commission will be reviewed by the Food and Drug Administration and will be accepted without change, accepted with change, or not accepted.

(b) Review of Codex standards will be accomplished in one of the following three ways:

(1) Any interested person may petition the Commissioner to adopt a

Codex standard, with or without change, by proposing a new standard or an appropriate amendment of an existing standard, pursuant to section 401 of the Act. Any such petition shall specify any deviations from the Codex standard, and the reasons for any such deviations. The Commissioner shall publish such a petition in the *FEDERAL REGISTER* as a proposal, with an opportunity for comment, if reasonable grounds are provided in the petition. Any published proposal shall state any deviations from the Codex standard and the stated reasons therefor.

(2) The Commissioner may on his own initiative propose by publication in the *FEDERAL REGISTER* the adoption of a Codex standard, with or without change, through a new standard or an appropriate amendment to an existing standard, pursuant to section 401 of the Act. Any such proposal shall specify any deviations from the Codex standard, and the reasons for any such deviations.

(3) Any Codex standard not handled under paragraph (b) (1) or (2) of this section may be published in the *FEDERAL REGISTER* for review and informal comment. Interested persons shall be requested to comment on the desirability and need for the standard, on the specific provisions of the standard, on additional or different provisions that should be included in the standard, and on any other pertinent points. After reviewing all such comments, the Commissioner either shall publish a proposal to establish a food standard pursuant to section 401 of the Act covering the food involved, or shall publish a notice terminating consideration of such a standard.

(c) All interested persons are encouraged to confer with different interest groups (consumers, industry, the academic community, professional organizations, and others) in formulating petitions or comments pursuant to paragraph (b) of this section. All such petitions or comments are requested to include a statement of any meetings and discussions that have been held with other interest groups. Appropriate weight will be given by the Commissioner to petitions or comments that reflect a consensus of different interest groups.

§ 564.8 Conformity to definitions and standards of identity.

In the following conditions, among others, a food does not conform to the definition and standard of identity therefor:

(a) If it contains an ingredient for which no provision is made in such definition and standard, unless such ingredient is an incidental additive introduced at a nonfunctional and insignificant level as a result of its deliberate and purposeful addition to another ingredient permitted by the terms of the applicable standard and the presence of such incidental additive in unstandardized foods has been exempted from label declaration as provided in § 501.100 of this chapter.

(b) If it fails to contain any one or more ingredients required by such definition and standard;

(c) If the quantity of any ingredient or component fails to conform to the limitation, if any, prescribed therefor by such definition and standard.

§ 564.12 General methods for water capacity and fill of container.

For the purposes of regulations promulgated under section 401 of the Act:

(a) The term "general method for water capacity of containers" means the following method:

(1) In the case of a container with lid attached by double seam, cut out the lid without removing or altering the height of the double seam.

(2) Wash, dry, and weigh the empty container.

(3) Fill the container with distilled water at 68° F to $\frac{1}{8}$ inch vertical distance below the top level of the container, and weigh the container thus filled.

(4) Subtract the weight found in paragraph (a)(2) of this section from the weight found in paragraph (a)(3) of this section. The difference shall be considered to be the weight of water required to fill the container.

In the case of a container with lid attached otherwise than by double seam, remove the lid and proceed as directed in paragraph (a)(2) to (4) of this section, except that under paragraph (a)(3) of this section, fill the container to the level of the top thereof.

(b) The term "general method for fill of containers" means the following method:

(1) In the case of a container with lid attached by double seam, cut out the lid without removing or altering the height of the double seam.

(2) Measure the vertical distance from the top level of the container to the top level of the food.

(3) Remove the food from the container; wash, dry, and weigh the container.

(4) Fill the container with water to $\frac{1}{8}$ inch vertical distance below the top level of the container. Record the temperature of the water, weigh the container thus filled, and determine the weight of the water by subtracting the weight of the container found in paragraph (b)(3) of this section.

(5) Maintaining the water at the temperature recorded in paragraph (b)(4) of this section, draw off water from the container as filled in paragraph (b)(4) of this section to the level of the food found in paragraph (b)(2) of this section, weigh the container with remaining water, and determine the weight of the remaining water by subtracting the weight of the container found in paragraph (b)(3) of this section.

(6) Divide the weight of water found in paragraph (b)(5) of this section by the weight of water found in paragraph (b)(4) of this section, and multiply by 100. The result shall be considered to be the percent of the total capacity of the container occupied by the food.

In the case of a container with lid attached otherwise than by double seam, remove the lid and proceed as directed in paragraph (b)(2) to (6) of this section, except that under paragraph (b)(4) of this section, fill the container to the level of the top thereof.

§ 564.14 General statements of substandard quality and substandard fill of container.

For the purposes of regulations promulgated under section 401 of the Act:

(a) The term "general statement of substandard quality" means the statement "Below Standard in Quality Good Food—Not High Grade" printed in two lines of Cheltenham bold condensed caps. The words "Below Standard in Quality" constitute the first line, and the second immediately follows. If the quantity of the contents of the container is less than 1 pound, the type of the first line is 12-point and of the second, 8-point. If such quantity is 1 pound or more, the type of the first line is 14-point, and of the second, 10-point. Such statement is enclosed within lines, not less than 6 points in width, forming a rectangle. Such statement, with enclosing lines, is on a strongly contrasting, uniform background, and is so placed as to be easily seen when the name of the food or any pictorial representation thereof is viewed, wherever such name or representation appears so conspicuously as to be easily seen under customary conditions of purchase.

(b) The term "general statement of substandard fill" means the statement "Below Standard in Fill" printed in Cheltenham bold condensed caps. If the quantity of the contents of the container is less than 1 pound, the statement is in 12-point type; if such quantity is 1 pound or more, the statement is in 14-point type. Such statement is enclosed within lines, not less than 6 points in width, forming a rectangle; but if the statement specified in paragraph (a) of this section is also used, both statements (one following the other) may be enclosed within the same rectangle. Such statement or statements, with enclosing lines, are on a strongly contrasting, uniform background, and are so placed as to be easily seen when the name of the food or any pictorial representation thereof is viewed, wherever such name or representation appears so conspicuously as to be easily seen under customary conditions of purchase.

§ 564.17 Temporary permits for interstate shipment of experimental packs of food varying from the requirements of definitions and standards of identity.

(a) The Food and Drug Administration recognizes that before petitions to amend food standards can be submitted, appropriate investigations of potential advances in food technology sometimes require tests in interstate markets of the advantages to and ac-

ceptance by consumers of experimental packs of food varying from applicable definitions and standards of identity prescribed under section 401 of the Act.

(b) It is the purpose of the Administration to permit such tests when it can be ascertained that the sole purpose of the tests is to obtain data necessary for reasonable grounds in support of a petition to amend food standards, that the tests are necessary to the completion or conclusiveness of an otherwise adequate investigation, and that the interests of consumers are adequately safeguarded; permits for such tests shall normally be for a period not to exceed 15 months. The Commissioner, for good cause shown by the applicant, may provide for a longer test market period. The Administration will therefore refrain from recommending regulatory proceedings under the Act on the charge that a food does not conform to an applicable standard, if the person who introduces or causes the introduction of the food into interstate commerce holds an effective permit from the Commissioner providing specifically for those variations in respect to which the food fails to conform to the applicable definition and standard of identity. The test period will begin on the date the person holding an effective permit from the Commissioner introduces or causes the introduction of the food covered by the permit into interstate commerce but no later than 3 months after notice of the issuance of the permit is published in the FEDERAL REGISTER. The Commissioner shall be notified in writing of the date on which the test period begins as soon as it is determined.

(c) Any person desiring a permit may file with the Commissioner a written application in triplicate containing as part thereof the following:

- (1) Name and address of the applicant.
- (2) A statement of whether or not the applicant is regularly engaged in producing the food involved.
- (3) A reference to the applicable definition and standard of identity (citing applicable section of regulations).
- (4) A full description of the proposed variation from the standard.

(5) The basis upon which the food so varying is believed to be wholesome and nondeleterious.

(6) The amount of any new ingredient to be added; the amount of any ingredient, required by the standard, to be eliminated; any change of concentration not contemplated by the standard; or any change in name that would more appropriately describe the new product under test. If such new ingredient is not a commonly known food ingredient, a description of its properties and basis for concluding that it is not a deleterious substance.

(7) The purpose of effecting the variation.

(8) A statement of how the variation is of potential advantage to consumers. The statement shall include the reasons why the applicant does not consider the data obtained in any prior investigations which may have been conducted sufficient to support a petition to amend the standard.

(9) The proposed label (or an accurate draft) to be used on the food to be market tested. The label shall conform in all respects to the general requirements of the Act and shall provide a means whereby the consumer can distinguish between the food being tested and such food complying with the standard.

(10) The period during which the applicant desires to introduce such food into interstate commerce, with a statement of the reasons supporting the need for such period. If a period longer than 15 months is requested, a detailed explanation of why a 15-month period is inadequate shall be provided.

(11) The probable amount of such food that will be distributed. The amount distributed should be limited to the smallest number of units reasonably required for a bona fide market test. Justification for the amount requested shall be included.

(12) The areas of distribution.

(13) The address at which such food will be manufactured.

(14) A statement of whether or not such food has been or is to be distributed in the State in which it was manufactured.

(15) If it has not been or is not to be so distributed, a statement showing why.

(16) If it has been or is to be so distributed, a statement of why it is deemed necessary to distribute such food in other States.

(d) The Commissioner may require the applicant to furnish samples of the food varying from the standard and to furnish such additional information as may be deemed necessary for action on the application.

(e) If the Commissioner concludes that the variation may be advantageous to consumers and will not result in failure of the food to conform to any provision of the Act except section 403(g), a permit shall be issued to the applicant for interstate shipment of such food. The terms and conditions of the permit shall be those set forth in the application with such modifications, restrictions, or qualifications as the Commissioner may deem necessary and state in the permit.

(f) The terms and conditions of the permit may be modified at the discretion of the Commissioner or upon application of the permittee during the effective period of the permit.

(g) The Commissioner may revoke a permit for cause, which shall include but not be limited to the following:

(1) That the permittee has introduced a food into interstate commerce contrary to the terms and conditions of the permit.

(2) That the application for a permit contains an untrue statement of a material fact.

(3) That the need therefor no longer exists.

(h) During the period within which any permit is effective, it shall be deemed to be included within the terms of any guaranty or undertaking otherwise effective pursuant to the provisions of section 303(c) of the Act.

(i) If an application is made for an extension of the permit, it shall be accompanied by a description of experiments conducted under the permit, tentative conclusions reached, and reasons why further experimental shipments are considered necessary. The application for an extension shall be filed not later than 3 months prior to the expiration date of the permit and

shall be accompanied by a petition to amend the affected food standard. If the Commissioner concludes that it will be in the interest of consumers to issue an extension of the time period for the market test, a notice will be published in the *FEDERAL REGISTER* stating that fact. The notice will include an invitation to all interested persons to participate in the market test under the same conditions that applied to the initial permit holder, including labeling and the amount to be distributed, except that the designated area of distribution shall not apply. The extended market test period shall not begin prior to the publication of a notice in the *FEDERAL REGISTER* granting the extension and shall terminate either on the effective date of an affirmative order ruling on the proposal or 30 days after a negative order ruling on the proposal, whichever the case may be. Any interested person who accepts the invitation to participate in the extended market test shall notify the Commissioner in writing of that fact, the amount to be distributed, and the area of distribution; and along with such notification, he shall submit the labeling under which the food is to be distributed.

(j) Notice of the granting or revocation of any permit shall be published in the *FEDERAL REGISTER*.

(k) All applications for a temporary permit, applications for an extension of a temporary permit, and related records are available for public disclosure when the notice of a permit or extension thereof is published in the *FEDERAL REGISTER*. Such disclosure shall be in accordance with the rules established in Part 4 of this chapter.

(l) Any person who contests denial, modification, or revocation of a temporary permit shall have an opportunity for a regulatory hearing before the Food and Drug Administration pursuant to Part 16 of this chapter.

[41 FR 38641, Sept. 10, 1976, as amended at 42 FR 4717, Jan. 25, 1977; 42 FR 15675, Mar. 22, 1977]

Subpart B—Food Additives in Standardized Animal Food

§ 570.20 Food additives proposed for use in animal foods for which definitions and standards of identity are established.

(a) Where a petition is received for the issuance or amendment of a regulation establishing a definition and standard of identity for a food under section 401 of the Act, which proposes the inclusion of a food additive in such definition and standard of identity, the provisions of the regulations in this subchapter E shall apply with respect to the information that must be submitted with respect to the food additive. Since section 409(b)(5) of the Act requires that the Commissioner publish notice of a petition for the establishment of a food-additive regulation within 30 days after filing, notice of a petition relating to a definition and standard of identity shall also be published within that time limitation if it includes a request, so designated, for the establishment of a regulation pertaining to a food additive.

(b) If a petition for a definition and standard of identity contains a proposal for a food-additive regulation, and the petitioner fails to designate it as such, the Commissioner, upon determining that the petition includes a proposal for a food-additive regulation, shall so notify the petitioner and shall thereafter proceed in accordance with the regulations in this Subchapter E.

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570.17 Exemption for investigational use and procedure for obtaining authorization to market edible products from experimental animals.

570.18 Tolerances for related food additives.

570.19 Pesticide chemicals in processed foods.

Subpart B—Food Additive Safety

570.20 General principles for evaluating the safety of food additives.

570.22 Safety factors to be considered.

570.30 Eligibility for classification as generally recognized as safe (GRAS).

570.35 Affirmation of generally recognized as safe (GRAS) status.

570.38 Determination of food additive status.

AUTHORITY: Secs. 201(s), 409, 72 Stat. 1784-1788 as amended (21 U.S.C. 321(s), 348); 21 CFR 5.10, 5.61.

SOURCE: 41 FR 38644, Sept. 10, 1976, unless otherwise noted.

Subpart A—General Provisions**§ 570.3 Definitions.**

(a) "Secretary" means the Secretary of Health and Human Services.

(b) "Department" means the Department of Health and Human Services.

(c) "Commissioner" means the Commissioner of Food and Drugs.

(d) As used in this part, the term "Act" means the Federal Food, Drug, and Cosmetic Act approved June 25, 1936 (52 Stat. 1040 et seq., as amended; 21 U.S.C. 301-392).

(e) "Food additives" includes all substances not exempted by section 201(s) of the Act, the intended use of which results or may reasonably be expected to result, directly or indirectly, either in their becoming a component of food or otherwise affecting the characteristics of food. A material used in the production of containers and packages is subject to the definition if it may reasonably be expected to become a component, or to affect the characteristics, directly or indirectly, of food packed in the container. "Affecting the characteristics of food" does not include such physical effects, as protecting contents of packages, preserving shape, and preventing moisture loss. If there is no migration of a pack-

PART 570—FOOD ADDITIVES**Subpart A—General Provisions**

- 1. Definitions.
- 2. Opinion letters on food additive status.
- 3. Indirect food additives resulting from packaging materials prior sanctioned for animal feed and pet food.
- 4. Indirect food additives resulting from packaging materials for animal feed and pet food.
- 5. Adoption of regulation on initiative of Commissioner.

aging component from the package to the food, it does not become a component of the food and thus is not a food additive. A substance that does not become a component of food, but that is used, for example, in preparing an ingredient of the food to give a different flavor, texture, or other characteristic in the food, may be a food additive.

(f) "Common use in food" means a substantial history of consumption of a substance by a significant number of animals in the United States.

(g) The word "substance" in the definition of the term "food additive" includes a food or feed or a component of a food or feed consisting of one or more ingredients.

(h) "Scientific procedures" include those human, animal, analytical, and other scientific studies, whether published or unpublished, appropriate to establish the safety of a substance.

(i) "Safe" or "safety" means that there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use. It is impossible in the present state of scientific knowledge to establish with complete certainty the absolute harmlessness of the use of any substance. Safety may be determined by scientific procedures or by general recognition of safety. In determining safety, the following factors shall be considered:

(1) The probable consumption of the substance and of any substance formed in or on food because of its use;

(2) The cumulative effect of the substance in the diet, taking into account any chemically or pharmacologically related substance or substances in such diet;

(3) Safety factors which, in the opinion of experts qualified by scientific training and experience to evaluate the safety of food and food ingredients, are generally recognized as appropriate.

(j) The term "nonperishable processed food" means any processed food not subject to rapid decay or deterioration that would render it unfit for consumption. Not included are hermetically sealed foods and other processed foods requiring refrigeration.

(k) "General recognition of safety" shall be determined in accordance with § 570.30.

(l) "Prior sanction" means an explicit approval granted with respect to use of a substance in food prior to September 6, 1958, by the Food Drug and Administration or the United States Department of Agriculture pursuant to the Federal Food, Drug, and Cosmetic Act, the Poultry Products Inspection Act, or the Meat Inspection Act.

(m) "Food" includes human food, substances migrating to food from food-contact articles, pet food, and animal feed.

(Secs. 201(s) 402, 409, 701(a), 52 Stat. 1048-1047 as amended, 1055, 72 Stat. 1784-1788 as amended (21 U.S.C. 321(s), 342, 348, 371(a)))

[41 FR 38644, Sept. 10, 1976, as amended at 42 FR 55206, Oct. 14, 1977]

§ 570.6 Opinion letters on food additive status.

(a) Over the years the Food and Drug Administration has given informal written opinions to inquirers as to the safety of articles intended for use as components of, or in contact with, food. Prior to the enactment of the Food Additives Amendment of 1958 (Public Law 85-929, Sept. 6, 1958), these opinions were given pursuant to section 402(a)(1) of the Federal Food, Drug, and Cosmetic Act, which reads in part: "A food shall be deemed to be adulterated if it bears or contains any poisonous or deleterious substance which may render it injurious to health".

(b) Since enactment of the Food Additives Amendment, the Food and Drug Administration has advised such inquirers that an article:

(1) Is a food additive within the meaning of section 201(s) of the Act; or

(2) Is generally recognized as safe (GRAS); or

(3) Has prior sanction or approval under that amendment; or

(4) Is not a food additive under the conditions of intended use.

(c) In the interest of the public health, such articles which have been considered in the past by the Food and Drug Administration to be safe under the provisions of section 402(a)(1), or

to be generally recognized as safe for their intended use, or to have prior sanction or approval, or not to be food additives under the conditions of intended use, must be reexamined in the light of current scientific information and current principles for evaluating the safety of food additives if their use is to be continued.

(d) Because of the time span involved, copies of many of the letters in which the Food and Drug Administration has expressed an informal opinion concerning the status of such articles may no longer be in the file of the Food and Drug Administration. In the absence of information concerning the names and uses made of all the articles referred to in such letters, their safety of use cannot be reexamined. For this reason all food additive status opinions of the kind described in paragraph (c) of this section given by the Food and Drug Administration are hereby revoked.

(e) The prior opinions of the kind described in paragraph (c) of this section will be replaced by qualified and current opinions if the recipient of each such letter forwards a copy of each to the Department of Health and Human Services, Food and Drug Administration, Bureau of Veterinary Medicine, Office of Compliance (HFV-200), 5600 Fishers Lane, Rockville, MD 20852, along with a copy of his letter of inquiry, on or before July 23, 1970.

(f) This section does not apply to food additive status opinion letters pertaining to articles that were considered by the Food and Drug Administration to be food additives nor to articles included in regulations in this Subchapter E if the articles are used in accordance with the requirements of such regulations.

Sec. 201, 72 Stat. 1784-88, as amended; 21 U.S.C. 321)

§ 570.13 Indirect food additives resulting from packaging materials prior sanctioned for animal feed and pet food.

Regulations providing for the use of food packaging materials as prior sanctioned in Part 181 of this chapter are incorporated in Subchapter E as applicable to packaging materials used for animal feed and pet food.

[42 FR 14091, Mar. 15, 1977]

§ 570.14 Indirect food additives resulting from packaging materials for animal feed and pet food.

Regulations providing for the use of food packaging materials in Parts 174 through 179 of this chapter are incorporated in Subchapter E as applicable to packaging materials used for animal feed and pet food.

[42 FR 14091, Mar. 15, 1977]

§ 570.15 Adoption of regulation on initiative of Commissioner.

(a) The Commissioner upon his own initiative may propose the issuance of a regulation prescribing, with respect to any particular use of a food additive, the conditions under which such additive may be safely used. Notice of such proposal shall be published in the FEDERAL REGISTER and shall state the reasons for the proposal.

(b) Action upon a proposal made by the Commissioner shall proceed as provided in Part 10 of this chapter.

[41 FR 38644, Sept. 10, 1976, as amended at 42 FR 4717, Jan. 25, 1977; 42 FR 15675, Mar. 22, 1977]

§ 570.17 Exemption for investigational use and procedure for obtaining authorization to market edible products from experimental animals.

A food additive or food containing a food additive intended for investigational use by qualified experts shall be exempt from the requirements of section 409 of the Act under the following conditions:

(a) If intended for investigational use in vitro or in laboratory research animals, it bears a label which states prominently, in addition to the other information required by the Act, the warning:

Caution. Contains a new food additive for investigational use only in laboratory research animals or for tests in vitro. Not for use in humans.

(b) If intended for use in animals other than laboratory research animals and if the edible products of the animals are to be marketed as food, permission for the marketing of the edible products as food has been re-

quested by the sponsor, and authorization has been granted by the Food and Drug Administration in accordance with § 511.1 of this chapter or by the Department of Agriculture in accordance with 9 CFR 309.17, and it bears a label which states prominently, in addition to the other information required by the Act, the warning:

Caution. Contains a new food additive for use only in investigational animals. Not for use in humans.

Edible products of investigational animals are not to be used for food unless authorization has been granted by the U.S. Food and Drug Administration or by the U.S. Department of Agriculture.

(c) If intended for nonclinical laboratory studies in food-producing animals, the study is conducted in compliance with the regulations set forth in Part 58 of this chapter.

(Secs. 406, 408, 409, 502, 503, 505, 506, 507, 510, 512-516, 518-520, 601, 701(a), 706, and 801, 52 Stat. 1049-1053 as amended, 1055, 1058 as amended, 55 Stat. 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511-517 as amended, 72 Stat. 1785-1788 as amended, 76 Stat. 794 as amended, 82 Stat. 343-351, 90 Stat. 539-574 (21 U.S.C. 346, 346a, 348, 352, 353, 355, 356, 357, 360, 360b-360f, 360h-360i); secs. 215, 351, 354-360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended; 42 U.S.C. 216, 262, 263b-263n)

[41 FR 38644, Sept. 10, 1976, as amended at 43 FR 60023, Dec. 22, 1978]

§ 570.18 Tolerances for related food additives.

(a) Food additives that cause similar or related pharmacological effects will be regarded as a class, and in the absence of evidence to the contrary, as having additive toxic effects and will be considered as related food additives.

(b) Tolerances established for such related food additives may limit the amount of a common component that may be present, or may limit the amount of biological activity (such as cholinesterase inhibition) that may be present or may limit the total amount of related food additives that may be present.

(c) Where food additives from two or more chemicals in the same class are present in or on a food, the tolerance for the total of such additives shall be the same as that for the additive having the lowest numerical tolerance

in this class, unless there are available methods that permit quantitative determination of the amount of each food additive present or unless it is shown that a higher tolerance is reasonably required for the combined additives to accomplish the physical or technical effect for which such combined additives are intended and that the higher tolerance will be safe.

(d) Where residues from two or more additives in the same class are present in or on a food and there are available methods that permit quantitative determination of each residue, the quantity of combined residues that are within the tolerance may be determined as follows:

(1) Determine the quantity of each residue present.

(2) Divide the quantity of each residue by the tolerance that would apply if it occurred alone, and multiply by 100 to determine the percentage of the permitted amount of residue present.

(3) Add the percentages so obtained for all residues present.

(4) The sum of the percentages shall not exceed 100 percent.

§ 570.19 Pesticide chemicals in processed foods.

When pesticide chemical residues occur in processed foods due to the use of raw agricultural commodities that bore or contained a pesticide chemical in conformity with an exemption granted or a tolerance prescribed under section 408 of the Act, the processed food will not be regarded as adulterated so long as good manufacturing practice has been followed in removing any residue from the raw agricultural commodity in the processing (such as by peeling or washing) and so long as the concentration of the residue in the processed food when ready to eat is not greater than the tolerance prescribed for the raw agricultural commodity. But when the concentration of residue in the processed food when ready to eat is higher than the tolerance prescribed for the raw agricultural commodity, the processed food is adulterated unless the higher concentration is permitted by a tolerance obtained under section 409 of the Act. For example, if fruit bearing a

residue of 7 parts per million of DDT permitted on the raw agricultural commodity is dried and a residue in excess of 7 parts per million of DDT results on the dried fruit, the dehydrated fruit is adulterated unless the higher tolerance for DDT is authorized by the regulations in this part. Food that is itself ready to eat, and which contains a higher residue than allowed for the raw agricultural commodity, may not be legalized by blending or mixing with other foods to reduce the residue in the mixed food below the tolerance prescribed for the raw agricultural commodity.

Subpart B—Food Additive Safety

§ 570.20 General principles for evaluating the safety of food additives.

(a) In reaching a decision on any petition filed under section 409 of the Act, the Commissioner will give full consideration to the specific biological properties of the compound and the adequacy of the methods employed to demonstrate safety for the proposed use, and the Commissioner will be guided by the principles and procedures for establishing the safety of food additives stated in current publications of the National Academy of Sciences-National Research Council. A petition will not be denied, however, by reason of the petitioner's having followed procedures other than those outlined in the publications of the National Academy of Sciences-National Research Council if, from available evidence, the Commissioner finds that the procedures used give results as reliable as, or more reliable than, those reasonably to be expected from the use of the outlined procedures. In reaching a decision, the Commissioner will give due weight to the anticipated levels and patterns of consumption of the additive specified or reasonably inferable. For the purposes of this section, the principles for evaluating safety of additives set forth in the above-mentioned publications will apply to any substance that may properly be classified as a food additive as defined in section 201(s) of the Act.

(b) Upon written request describing the proposed use of an additive and the proposed experiments to deter-

mine its safety, the Commissioner will advise a person who wishes to establish the safety of a food additive whether he believes the experiments planned will yield data adequate for an evaluation of the safety of the additive.

§ 570.22 Safety factors to be considered.

In accordance with section 409(c)(5)(C) of the Act, the following safety factors will be applied in determining whether the proposed use of a food additive will be safe: Except where evidence is submitted which justifies use of a different safety factor, a safety factor in applying animal experimentation data to man of 100 to 1, will be used; that is, a food additive for use by man will not be granted a tolerance that will exceed $\frac{1}{100}$ th of the maximum amount demonstrated to be without harm to experimental animals.

§ 570.30 Eligibility for classification as generally recognized as safe (GRAS).

(a) General recognition of safety may be based only on the views of experts qualified by scientific training and experience to evaluate the safety of substances directly or indirectly added to food. The basis of such views may be either (1) scientific procedures or (2) in the case of a substance used in food prior to January 1, 1958, through experience based on common use in food. General recognition of safety requires common knowledge about the substance throughout the scientific community knowledgeable about the safety of substances directly or indirectly added to food.

(b) General recognition of safety based upon scientific procedures shall require the same quantity and quality of scientific evidence as is required to obtain approval of a food additive regulation for the ingredient. General recognition of safety through scientific procedures shall ordinarily be based upon published studies which may be corroborated by unpublished studies and other data and information.

(c) General recognition of safety through experience based on common use in food prior to January 1, 1958, may be determined without the quan-

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tity or quality of scientific procedures required for approval of a food additive regulation. General recognition of safety through experience based on common use in food prior to January 1, 1958, shall ordinarily be based upon generally available data and information. An ingredient not in common use in food prior to January 1, 1958, may achieve general recognition of safety only through scientific procedures.

(d) The food ingredients listed as GRAS in Part 582 of this chapter do not include all substances that are generally recognized as safe for their intended use in food. Because of the large number of substances the intended use of which results or may reasonably be expected to result, directly or indirectly, in their becoming a component or otherwise affecting the characteristics of food, it is impracticable to list all such substances that are GRAS. A food ingredient of natural biological origin that has been widely consumed for its nutrient properties in the United States prior to January 1, 1958, without known detrimental effects, which is subject only to conventional processing as practiced prior to January 1, 1958, and for which no known safety hazard exists, will ordinarily be regarded as GRAS without specific inclusion in Part 582 of this chapter.

(e) A food ingredient that is not GRAS or subject to a prior sanction requires a food additive regulation promulgated under section 409 of the Act before it may be directly or indirectly added to food.

(f) A food ingredient that is listed as GRAS in Part 582 of this chapter shall be regarded as GRAS only if, in addition to all the requirements in the applicable regulation, it also meets all of the following requirements:

(1) It complies with any applicable specifications, or in the absence of such specifications, shall be of a purity suitable for its intended use.

(2) It performs an appropriate function in the food or food-contact article in which it is used.

(3) It is used at a level no higher than necessary to achieve its intended purpose in that food or, if used as a component of a food-contact article, at a level no higher than necessary to

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achieve its intended purpose in that article.

(g) New information may at any time require reconsideration of the GRAS status of a food ingredient. Any change in status shall be accomplished pursuant to § 570.38.

(h) If a substance is affirmed as GRAS pursuant to § 570.35 and listed in a regulation with no limitation other than good manufacturing practice, it shall be regarded as GRAS if its conditions of use are not significantly different from those reported in the regulation as the basis on which the GRAS status of the substance was affirmed. If the conditions of use are significantly different, such use of the substance may not be GRAS. In such case a manufacturer may not rely on the regulation as authorizing the use but must independently establish that the use is GRAS or must use the substance in accordance with a food additive regulation.

(i) If an ingredient is affirmed as GRAS pursuant to § 570.35 and listed in a regulation with specific limitation(s), it may be used in food only within such limitation(s) (including the category of food(s), the functional use(s) of the ingredient, and the level(s) of use). Any use of such ingredient not in full compliance with each such established limitation shall require a food additive regulation.

(j) Pursuant to § 570.35, a food ingredient may be affirmed as GRAS and listed in a regulation for a specific use(s) without a general evaluation of use of the ingredient. In addition to the use(s) specified in the regulation, other uses of such an ingredient may also be GRAS. Any affirmation of GRAS status for a specific use(s) without a general evaluation of use of the ingredient, is subject to reconsideration upon such evaluation.

(Secs. 201, 402, 409, 701(a), 52 Stat. 1946-1947 as amended, 1055, 72 Stat. 1784-1788 as amended (21 U.S.C. 321(a), 342, 348, 371(a)) [42 FR 55206, Oct. 14, 1977]

§ 570.35 Affirmation of generally recognized as safe (GRAS) status.

(a) The Commissioner, either on his initiative or on the petition of an interested person, may affirm the GRAS

status of substances that directly or indirectly become components of food.

(b)(1) If the Commissioner proposes on his own initiative that a substance is entitled to affirmation as GRAS, he will place all of the data and information on which he relies on public file in the office of the Dockets Management Branch and will publish in the FEDERAL REGISTER a notice giving the name of the substance, its proposed uses, and any limitations proposed for purposes other than safety.

(2) The FEDERAL REGISTER notice will allow a period of 60 days during which any interested person may review the data and information and/or file comments with the Dockets Management Branch. Copies of all comments received shall be made available for examination in the Dockets Management Branch's office.

(3) The Commissioner will evaluate all comments received. If he concludes that there is convincing evidence that the substance is GRAS as defined in § 570.3(k), he will publish a notice in the FEDERAL REGISTER listing the substance in this Subchapter E as GRAS.

(4) If, after evaluation of the comments, the Commissioner concludes that there is a lack of convincing evidence that the substance is GRAS and that it should be considered a food additive subject to section 409 of the Act, he shall publish a notice thereof in the FEDERAL REGISTER in accordance with § 570.38.

(c)(1) Persons seeking the affirmation of GRAS status of substances as provided for in § 570.30(e), except those subject to the NAS-NRC GRAS list survey (36 FR 20546), shall submit a petition for GRAS affirmation pursuant to Part 10 of this chapter. Such petition shall contain information to establish that the GRAS criteria as set forth in § 570.30(b) have been met, in the following form:

(i) Description of the substance, including:

- (a) Common or usual name.
- (b) Chemical name.
- (c) Chemical Abstract Service (CAS) registry number.
- (d) Empirical formula.
- (e) Structural formula.
- (f) Specifications for food grade material, including arsenic and heavy

metals. (Recommendation for any change in the Food Chemicals Codex monograph should be included where applicable.)

(g) Quantitative compositions.

(h) Manufacturing process (excluding any trade secrets).

(ii) Use of the substance, including:

(a) Date when use began.

(b) Information and reports or other data on past uses in food.

(c) Foods in which used, and levels of use in such foods, and for what purposes.

(iii) Methods for detecting the substance in food, including:

(a) References to qualitative and quantitative methods for determining the substance(s) in food, including the type of analytical procedures used.

(b) Sensitivity and reproducibility of such method(s).

(iv) Information to establish the safety and functionality of the substance in food. Published scientific literature, evidence that the substance is identical to a GRAS counterpart of natural biological origin, and other data may be submitted to support safety. Any adverse information or consumer complaints shall be included. Complete bibliographic references shall be provided where a copy of the article is not provided.

(v) A statement signed by the person responsible for the petition that to the best of his knowledge it is a representative and balanced submission that includes unfavorable information, as well as favorable information, known to him pertinent to the evaluation of the safety and functionality of the substance.

(vi) If nonclinical laboratory studies are involved, additional information and data submitted in support of filed petitions shall include, with respect to each nonclinical study, either a statement that the study was conducted in compliance with the requirements set forth in Part 58 of this chapter, or, if the study was not conducted in compliance with such regulations, a brief statement of the reason for the non-compliance.

(vii) [Reserved]

(viii) A claim for categorical exclusion under § 25.24 of this chapter or

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an environmental assessment under § 25.31 of this chapter.

(2) Within 30 days after the date of filing the petition, the Commissioner will place the petition on public file in the office of the Hearing Clerk and will publish a notice of filing in the *FEDERAL REGISTER* giving the name of the petitioner and a brief description of the petition including the name of the substance, its proposed use, and any limitations proposed for reasons other than safety. A copy of the notice will be mailed to the petitioner at the time the original is sent to the *FEDERAL REGISTER*.

(3) The notice of filing in the *FEDERAL REGISTER* will allow a period of 60 days during which any interested person may review the petition and/or file comments with the Hearing Clerk. Copies of all comments received shall be made available for examination in the Hearing Clerk's office.

(4) The Commissioner will evaluate the petition and all available information including all comments received. If the petition and such information provide convincing evidence that the substance is GRAS as defined in § 570.3, he will publish an order in the *FEDERAL REGISTER* listing the substance in this Subchapter E as GRAS.

(5) If, after evaluation of the petition and all available information, the Commissioner concludes that there is a lack of convincing evidence that the substance is GRAS and that it should be considered a food additive subject to section 409 of the Act, he shall publish a notice thereof in the *FEDERAL REGISTER* in accordance with § 570.38.

(6) The notice of filing in the *FEDERAL REGISTER* will request submission of proof of any applicable prior sanction for use of the ingredient under conditions different from those proposed to be determined to be GRAS. The failure of any person to come forward with proof of such an applicable prior sanction in response to the notice of filing will constitute a waiver of the right to assert or rely on such sanction at any later time. The notice of filing will also constitute a proposal to establish a regulation under this Subchapter E, incorporating the same provisions, in the event that such a regulation is determined to be appropriate as

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a result of submission of proof of such an applicable prior sanction in response to the notice of filing.

(Secs. 201(a), 402, 409, 701(a), 52 Stat. 1046-1047 as amended, 1055, 72 Stat. 1784-1788 as amended (21 U.S.C. 321(a), 342, 346, 371(a)); secs. 406, 408, 409, 501, 502, 503, 505, 506, 507, 510, 512-516, 518-520, 601, 701, 706, and 801, 52 Stat. 1049-1053 as amended, 1055, 1056 as amended, 1058 as amended, 55 Stat. 851 as amended, 59 Stat. 463 as amended, 60 Stat. 511-517 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 399-407 as amended, 76 Stat. 794 as amended, 82 Stat. 343-351, 80 Stat. 539-574 (21 U.S.C. 346, 346a, 348, 351, 352, 353, 355, 356, 257, 360, 360b-360f, 360h-360i, 371, 376); secs. 215, 301, 351, 354-360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 241, 362, 263b-263n))

[41 FR 38644, Sept. 10, 1976, as amended at 42 FR 4717, Jan. 25, 1977; 42 FR 15675, Mar. 22, 1977; 42 FR 55207, Oct. 10, 1977; 50 FR 7517, Feb. 22, 1985; 50 FR 16668, Apr. 26, 1985]

§ 570.38 Determination of food additive status.

(a) The Commissioner may, in accordance with § 570.35 (b)(4) or (c)(5), publish a notice in the *FEDERAL REGISTER* determining that a substance is not GRAS and is a food additive subject to section 409 of the Act.

(b)(1) The Commissioner, on his own initiative or on the petition of any interested person, pursuant to Part 10 of this chapter, may issue a notice in the *FEDERAL REGISTER* proposing to determine that a substance is not GRAS and is a food additive subject to section 409 of the Act. Any petition shall include all relevant data and information of the type described in § 571.130(b) of this chapter. The Commissioner will place all of the data and information on which he relies on public file in the office of the Hearing Clerk and will include in the *FEDERAL REGISTER* notice the name of the substance, its known uses, and a summary of the basis for the determination.

(2) The *FEDERAL REGISTER* notice will allow a period of 60 days during which any interested person may review the data and information and/or file comments with the Hearing Clerk. Copies of all comments shall be made available for examination in the Hearing Clerk's office.

(3) The Commissioner will evaluate all comments received. If he concludes that there is a lack of convincing evidence that the substance is GRAS or is otherwise exempt from the definition of a food additive in section 201(s) of the Act, he will publish a notice thereof in the FEDERAL REGISTER. If he concludes that there is convincing evidence that the substance is GRAS, he will publish an order in the FEDERAL REGISTER listing the substance in this Subchapter E as GRAS.

(c) A FEDERAL REGISTER notice determining that a substance is a food additive shall provide for the use of the additive in food or food-contact surfaces as follows:

(1) It may promulgate a food additive regulation governing use of the additive.

(2) It may promulgate an interim food additive regulation governing use of the additive.

(3) It may require discontinuation of the use of the additive.

(4) It may adopt any combination of the above three approaches for different uses or levels of use of the additive.

(d) If the Commissioner of Food and Drugs is aware of any prior sanction for use of the substance, he will concurrently propose a separate regulation covering such use of the ingredient under this Subchapter E. If the Commissioner is unaware of any such applicable prior sanction, the proposed regulation will so state and will require any person who intends to assert or rely on such sanction to submit proof of its existence. Any regulation promulgated pursuant to this section constitutes a determination that excluded uses would result in adulteration of the food in violation of section 402 of the Act, and the failure of any person to come forward with proof of such an applicable prior sanction in response to the proposal will constitute a waiver of the right to assert or rely on such sanction at any later time. The notice will also constitute a proposal to establish a regulation under this Subchapter E., incorporating the same provisions, in the event that such a regulation is determined to be appropriate as a result of submission

of proof of such an applicable prior sanction in response to the proposal.

(Secs. 201(s), 402, 409, 701(a), 52 Stat. 1046-1047 as amended, 1055, 72 Stat. 1784-1788 as amended (21 U.S.C. 321(s), 342, 348, 371(a))) [41 FR 38644, Sept. 10, 1976, as amended at 42 FR 4717, Jan. 25, 1977; 42 FR 15675, Mar. 22, 1977; 42 FR 55207, Oct. 14, 1977]

PART 571—FOOD ADDITIVE PETITIONS

Subpart A—General Provisions

Sec.

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Subpart B—Administrative Actions on Applications

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571.110 Procedure for objections and hearings.

571.115 Application of the cancer clause of section 409 of the act.

571.130 Procedure for amending and repealing tolerances or exemptions from tolerances.

AUTHORITY: Secs. 409, 701, 52 Stat. 1055-1056 as amended, 72 Stat. 1785-1788 as amended (21 U.S.C. 348, 371).

SOURCE: 41 FR 38647, Sept. 10, 1976, unless otherwise noted.

Subpart A—General Provisions

§ 571.1 Petitions.

(a) Petitions to be filed with the Commissioner under the provisions of section 409(b) of the Act shall be submitted in triplicate. If any part of the material submitted is in a foreign language, it shall be accompanied by an accurate and complete English translation. The petition shall state petitioner's post office address to which published notices or orders issued or objections filed pursuant to section 409 of the Act may be sent.

(b) Pertinent information may be incorporated in, and will be considered as part of, a petition on the basis of specific reference to such information submitted to and retained in the files of the Food and Drug Administration. However, any reference to unpub-

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lished information furnished by a person other than the applicant will not be considered unless use of such information is authorized in a written statement signed by the person who submitted it. Any reference to published information offered in support of a food-additive petition should be accompanied by reprints or photostatic copies of such references.

(c) Petitions shall include the following data and be submitted in the following form:

(Date) _____
 Name of petitioner _____
 Post office address _____
 Date _____
 Name of food additive and proposed use _____

Food and Drug Administration
 CENTER FOR VETERINARY MEDICINE,
 Director, Division of Animal Feeds (HFV-
 220), 5600 Fishers Lane, Rockville, MD
 20857.

DEAR SIR: The undersigned, _____
 submits this petition pursuant to section
 409(b)(1) of the Federal Food, Drug, and
 Cosmetic Act with respect to _____

(Name of the food additive and proposed
 use)

Attached hereto, in triplicate, and constituting a part of this petition, are the following:

A. The name and all pertinent information concerning the food additive, including chemical identity and composition of the food additive, its physical, chemical, and biological properties, and specifications prescribing the minimum content of the desired component(s) and identifying and limiting the reaction byproducts and other impurities. Where such information is not available, a statement as to the reasons why it is not should be submitted.

When the chemical identity and composition of the food additive is not known, the petition shall contain information in sufficient detail to permit evaluation regarding the method of manufacture and the analytical controls used during the various stages of manufacturing, processing, or packing of the food additive which are relied upon to establish that it is a substance of reproducible composition. Alternative methods and controls and variations in methods and controls within reasonable limits that do not

affect the characteristics of the substance or the reliability of the controls may be specified.

If the food additive is a mixture of chemicals, the petition shall supply a list of all substances used in the synthesis, extraction, or other method of preparation, regardless of whether they undergo chemical change in the process. Each substance should be identified by its common English name and complete chemical name, using structural formulas when necessary for specific identification. If any proprietary preparation is used as a component, the proprietary name should be followed by a complete quantitative statement of composition. Reasonable alternatives for any listed substance may be specified.

If the petitioner does not himself perform all the manufacturing, processing, and packing operations for a food additive, the petition shall identify each person who will perform a part of such operations and designate the part.

The petition shall include stability data, and, if the data indicate that it is needed to ensure the identity, strength, quality, or purity of the additive, the expiration date that will be employed.

B. The amount of the food additive proposed for use and the purposes for which it is proposed, together with all directions, recommendations, and suggestions regarding the proposed use, as well as specimens of the labeling proposed for the food additive and any labeling that will be required by applicable provisions of the Federal Food, Drug, and Cosmetic Act on the finished food by reason of the use of the food additive. If the additive results or may reasonably be expected to result from the use of packaging material, the petitioner shall show how this may occur and what residues may reasonably be anticipated.

(Typewritten or other draft-labeling copy will be accepted for consideration of the petition, provided a statement is made that final printed labeling identical in content to the draft copy will be submitted as soon as available and prior to the marketing of the food additive.)

If the food additive is one for which a tolerance limitation is required to assure its safety, the level of use proposed should be no higher than the amount reasonably required to accomplish the intended physical or other technical effect, even though the safety data may support a higher tolerance.)

C. Data establishing that the food additive will have the intended physical or other technical effect or that it may reasonably be expected to become a component, or to affect the characteristics, directly or indirectly, of food and the amount necessary to accomplish this. These data should include

information in sufficient detail to permit evaluation with control data.

D. A description of practicable methods to determine the amount of the food additive in the raw, processed, and/or finished food and of any substance formed in or on such food because of its use. The test proposed shall be one that can be used for food-control purposes and that can be applied with consistent results by any properly equipped and trained laboratory personnel.

E. Full reports of investigations made with respect to the safety of the food additive.

(A petition may be regarded as incomplete unless it includes full reports of adequate tests reasonably applicable to show whether or not the food additive will be safe for its intended use. The reports ordinarily should include detailed data derived from appropriate animal and other biological experiments in which the methods used and the results obtained are clearly set forth. The petition shall not omit without explanation any reports of investigations that would bias an evaluation of the safety of the food additive.)

F. Proposed tolerances for the food additive, if tolerances are required in order to ensure its safety. A petitioner may include a proposed regulation.

G. If submitting petition to modify an existing regulation issued pursuant to section 409(c)(1)(A) of the act, full information on such proposed change that is to be made in the original regulation must be submitted. The petition may omit statements made in the original petition concerning which no change is proposed. A supplemental petition must be submitted for any change beyond the variations provided for in the original petition and the regulation issued on the basis of the original petition.

H. The petitioner is required to submit either a claim for categorical exclusion under § 25.24 of this chapter or an environmental assessment under § 25.31 of this chapter.

Yours very truly,
Petitioner _____
By _____
(Indicate authority)

(d) The petitioner will be notified of the date on which his petition is filed, and an incomplete petition, or one that has not been submitted in triplicate, will usually be retained but not filed as a petition under section 409 of the Act. The petitioner will be notified of what respects his petition is incomplete.

(e) The petition must be signed by the petitioner or by his attorney or agent, or (if a corporation) by an authorized official.

(f) The data specified under the several lettered headings should be submitted on separate sheets or sets of sheets, suitably identified. If such data have already been submitted with an earlier application, the present petition may incorporate it by specific reference to the earlier. If part of the data have been submitted by the manufacturer of the food additive as a master file, the petitioner may refer to the master file if and to the extent he obtains the manufacturer's written permission to do so. The manufacturer may authorize specific reference to the data without disclosure to the petitioner. Nothing herein shall prevent reference to published data.

(g) A petition shall be retained but shall not be filed if any of the data prescribed by section 409(b) of the Act are lacking or are not set forth so as to be readily understood.

(h)(1) The following data and information in a food additive petition are available for public disclosure, unless extraordinary circumstances are shown, after the notice of filing of the petition is published in the FEDERAL REGISTER or, if the petition is not promptly filed because of deficiencies in it, after the petitioner is informed that it will not be filed because of the deficiencies involved:

(i) All safety and functionality data and information submitted with or incorporated by reference in the petition.

(ii) A protocol for a test or study, unless it is shown to fall within the exemption established for trade secrets and confidential commercial information in § 20.61 of this chapter.

(iii) Adverse reaction reports, product experience reports, consumer complaints, and other similar data and information, after deletion of:

(a) Names and any information that would identify the person using the product.

(b) Names and any information that would identify any third party involved with the report, such as a physician or hospital or other institution.

(iv) A list of all ingredients contained in a food additive, whether or not it is in descending order of predominance. A particular ingredient or group of ingredients shall be deleted

from any such list prior to public disclosure if it is shown to fall within the exemption established in § 20.61 of this chapter, and a notation shall be made that any such ingredient list is incomplete.

(v) An assay method or other analytical method, unless it serves no regulatory or compliance purpose and is shown to fall within the exemption established in § 20.61 of this chapter.

(2) The following data and information in a food additive petition are not available for public disclosure unless they have been previously disclosed to the public as defined in § 20.81 of this chapter or they relate to a product or ingredient that has been abandoned and they no longer represent a trade secret or confidential commercial or financial information as defined in § 20.61 of this chapter:

(i) Manufacturing methods or processes, including quality control procedures.

(ii) Production, sales, distribution, and similar data and information, except that any compilation of such data and information aggregated and prepared in a way that does not reveal data or information which is not available for public disclosure under this provision is available for public disclosure.

(iii) Quantitative or semiquantitative formulas.

(3) All correspondence and written summaries of oral discussions relating to a food additive petition are available for public disclosure in accordance with the provisions of Part 20 of this chapter when the food additive regulation is published in the *FEDERAL REGISTER*.

(4) For purposes of this regulation, safety and functionality data include all studies and tests of a food additive on animals and humans and all studies and tests on a food additive for identity, stability, purity, potency, performance, and usefulness.

(i)(1) Within 15 days after receipt, the Commissioner will notify the petitioner of acceptance or nonacceptance of a petition, and if not accepted the reasons therefor. If accepted, the date of the notification letter sent to petitioner becomes the date of filing for the purposes of section 409(b)(5) of

the Act. If the petitioner desires, he may supplement a deficient petition after being notified regarding deficiencies. If the supplementary material or explanation of the petition is deemed acceptable, petitioner shall be notified. The date of such notification becomes the date of filing. If the petitioner does not wish to supplement or explain the petition and requests in writing that it be filed as submitted, the petition shall be filed and the petitioner so notified. The date of such notification becomes the date of filing.

(2) The Commissioner will publish in the *FEDERAL REGISTER* within 30 days from the date of filing of such petition, a notice of the filing, the name of the petitioner, and a brief description of the proposal in general terms. In the case of a food additive which becomes a component of food by migration from packaging material, the notice shall include the name of the migratory substance, and where it is different from that of one of the original components, the name of the parent component, the maximum quantity of the migratory substance that is proposed for use in food, and the physical or other technical effect which the migratory substance or its parent component is intended to have in the packaging material. A copy of the notice will be mailed to the petitioner when the original is forwarded to the *FEDERAL REGISTER* for publication.

(j) The Commissioner may request a full description of the methods used in, and the facilities and controls used for, the production of the food additive, or a sample of the food additive, articles used as components thereof, or of the food in which the additive is proposed to be used, at any time while a petition is under consideration. The Commissioner shall specify in the request for a sample of the food additive, or articles used as components thereof, or of the food in or on which the additive is proposed to be used, a quantity deemed adequate to permit tests of analytical methods to determine quantities of the food additive present in foods for which it is intended to be used or adequate for any study or investigation reasonably required with respect to the safety of

the food additive or the physical or technical effect it produces. The date used for computing the 90-day limit for the purposes of section 409(c)(2) of the Act shall be moved forward 1 day for each day after the mailing date of the request taken by the petitioner to submit the sample. If the information or sample is requested a reasonable time in advance of the 180 days, but is not submitted within such 180 days after filing of the petition, the petition will be considered withdrawn without prejudice.

(k) If nonclinical laboratory studies are involved, petitions filed with the Commissioner under section 409(b) of the Act shall include, with respect to each study, either a statement that the study was conducted in compliance with the requirements set forth in Part 56 of this chapter, or, if the study was not conducted in compliance with such regulations, a brief statement of the reason for the noncompliance.

(Secs. 406, 408, 409, 501, 502, 503, 505, 506, 507, 510, 512-516, 518-520, 601, 701, 706, and 801, 52 Stat. 1049-1053 as amended, 1055, 1056 as amended, 1058 as amended, 55 Stat. 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511-517 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 399-407 as amended, 76 Stat. 794 as amended, 82 Stat. 343-351, 90 Stat. 539-574 (21 U.S.C. 346, 346a, 348, 351, 352, 353, 355, 356, 357, 360, 360b-360f, 360h-360i, 371, 376); secs. 215, 301, 351, 354-360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 241, 262, 263b-263n))

(41 FR 38647, Sept. 10, 1976, as amended at 42 FR 15675, Mar. 22, 1977; 50 FR 7518, Feb. 22, 1985; 50 FR 16668, Apr. 26, 1985; 52 FR 8543, Mar. 19, 1987)

§ 571.6 Amendment of petition.

After a petition has been filed, the petitioner may submit additional information or data in support thereof. In such cases, if the Commissioner determines that the additional information or data amounts to a substantive amendment, the petition as amended will be given a new filing date, and the time limitation will begin to run anew. If nonclinical laboratory studies are involved, additional information and data submitted in support of filed petitions shall include, with respect to each such study, either a statement that the study was conducted in com-

pliance with the requirements set forth in Part 58 of this chapter, or, if the study was not conducted in compliance with such regulations, a brief statement of the reason or the non-compliance.

(Secs. 406, 408, 409, 501, 502, 503, 505, 506, 507, 510, 512-516, 518-520, 601, 701, 706, and 801, 52 Stat. 1049-1053 as amended, 1055, 1056 as amended, 1058 as amended, 55 Stat. 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511-517 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 399-407 as amended, 76 Stat. 794 as amended, 82 Stat. 343-351, 90 Stat. 539-574 (21 U.S.C. 346, 346a, 348, 351, 352, 353, 355, 356, 357, 360, 360b-360f, 360h-360i, 371, 376); secs. 215, 301, 351, 354-360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 241, 262, 263b-263n))

(41 FR 38647, Sept. 10, 1976, as amended at 50 FR 7518, Feb. 22, 1985; 50 FR 16668, Apr. 26, 1985)

§ 571.7 Withdrawal of petition without prejudice.

(a) In some cases the Commissioner will notify the petitioner that the petition, while technically complete, is inadequate to justify the establishment of a regulation or the regulation requested by petitioner. This may be due to the fact that the data are not sufficiently clear or complete. In such cases, the petitioner may withdraw the petition pending its clarification or the obtaining of additional data. This withdrawal will be without prejudice to a future filing. Upon refiling, the time limitation will begin to run anew from the date of refiling.

(b) At any time before the order provided for in § 571.100(a) has been forwarded to the FEDERAL REGISTER for publication, the petitioner may withdraw the petition without prejudice to a future filing. Upon refiling the time limitation will begin to run anew.

Subpart B—Administrative Actions on Applications

§ 571.100 Regulation based on petition.

(a) The Commissioner will forward for publication in the FEDERAL REGISTER, within 90 days after filing of the petition (or within 180 days if the time is extended as provided for in section 409(c)(2) of the Act), a regulation pre-

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scribing the conditions under which the food additive may be safely used (including, but not limited to, specifications as to the particular food or classes of food in or on which such additive may be used, the maximum quantity that may be used or permitted to remain in or on such food, the manner in which such additive may be added to or used in or on such food, and any directions or other labeling or packaging requirements for such additive deemed necessary by him to assure the safety of such use), and prior to the forwarding of the order to the FEDERAL REGISTER for publication shall notify the petitioner of such order and the reasons for such action; or by order deny the petition, and shall notify the petitioner of such order and of the reasons for such action.

(b) If the Commissioner determines that additional time is needed to study and investigate the petition, he shall by written notice to the petitioner extend the 90-day period for not more than 180 days after the filing of the petition.

§ 571.102 Effective date of regulation.

A regulation published in accordance with § 571.100(a) shall become effective upon publication in the FEDERAL REGISTER.

§ 571.110 Procedure for objections and hearings.

Objections and hearings relating to food additive regulations under section 409(c), (d), or (h) of the Act shall be governed by Part 12 of this chapter.

[42 FR 4717, Jan. 25, 1977, as amended at 42 FR 15676, Mar. 22, 1977]

§ 571.115 Application of the cancer clause of section 409 of the act.

Food additives intended for use as an ingredient in food for animals that are raised for food production and that have the potential to contaminate human food with residues whose consumption could present a risk of cancer to people must satisfy the requirements of Subpart E of Part 500 of this chapter.

[52 FR 49588, Dec. 31, 1987]

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§ 571.130 Procedure for amending and repealing tolerances or exemptions from tolerances.

(a) The Commissioner, on his own initiative or on the petition of any interested person, pursuant to Part 10 of this chapter, may propose the issuance of a regulation amending or repealing a regulation pertaining to a food additive or granting or repealing an exception for such additive.

(b) Any such petition shall include an assertion of facts, supported by data, showing that new information exists with respect to the food additive or that new uses have been developed or old uses abandoned, that new data are available as to toxicity of the chemical, or that experience with the existing regulation or exemption may justify its amendment or repeal. New data shall be furnished in the form specified in § 571.1 for submitting petitions.

[42 FR 4717, Jan. 25, 1977; 42 FR 15676, Mar. 22, 1977]

PART 573—FOOD ADDITIVES PERMITTED IN FEED AND DRINKING WATER OF ANIMALS

Subpart A—[Reserved]

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AUTHORITY: Secs. 201(s), 409, 72 Stat. 1784-1788 as amended (21 U.S.C. 321(s), 348); 21 CFR 5.10 and 5.61.

SOURCE: 41 FR 38652, Sept. 10, 1976, unless otherwise noted.

Subpart A—[Reserved]

Subpart B—Food Additive Listing

§ 573.120 Acrylamide-acrylic acid resin.

Acrylamide-acrylic acid resin (hydrolyzed polyacrylamide), only for the purposes of this section as described below, may be safely used in accordance with the following prescribed conditions:

(a) The additive is produced by polymerization of acrylamide with partial hydrolysis, or by copolymerization of acrylamide and acrylic acid with the greater part of the polymer being composed of acrylamide units.

(b) The additive meets the following specifications:

(1) A minimum molecular weight of 3 million.

(2) Viscosity range: 3,000 to 6,000 centipoises at 77° F in a 1 percent aqueous solution as determined by LVF Brookfield Viscometer or equivalent using a number 6 spindle at 20 r.p.m.

(3) Residual acrylamide: Not more than 0.05 percent.

(c) It is used as a thickener and suspending agent in nonmedicated aqueous suspensions intended for addition to animal feeds.

[41 FR 38652, Sept. 10, 1976, as amended at 45 FR 38058, June 6, 1980]

§ 573.140 Ammoniated cottonseed meal.

The food additive ammoniated cottonseed meal may be safely used in accordance with the following conditions:

(a) The food additive is the product obtained by the treatment of cottonseed meal with anhydrous ammonia until a pressure of 50 pounds per square inch gauge is reached.

(b) It is used or intended for use in the feed of ruminants as a source of protein and/or as a source of nonprotein nitrogen in an amount not to exceed 20 percent of the total ration.

(c) To assure safe use, the label and labeling of the additive and of any feed additive supplement, concentrate, or premix prepared therefrom shall bear, in addition to the other information required by the Act, the following:

(1) The name of the additive.

(2) The maximum percentage of equivalent crude protein from the nonprotein nitrogen.

(3) Directions for use to provide not more than 20 percent of the additive in the total ration.

(4) A statement:

(i) That not more than one-third of the total protein in the feed should come from nonprotein nitrogen sources.

(ii) That the additive is not to be given to debilitated or starved animals.

(iii) "Warning—This feed should be used only in accordance with directions furnished on the label."

[41 FR 38652, Sept. 10, 1976, as amended at 42 FR 52397, Sept. 30, 1977]

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§ 573.160 Ammoniated rice hulls.

The food additive ammoniated rice hulls may be safely used in accordance with the following prescribed conditions:

(a) The food additive is the product obtained by the treatment of ground rice hulls with monocalcium phosphate and anhydrous ammonia at a temperature of 350° F and a pressure of 175 pounds per square inch.

(b) It is used or intended for use in the feed of beef cattle as a source of crude fiber and as the sole source of nonprotein nitrogen in an amount not to exceed 20 percent of the total ration.

(c) To assure safe use of the additive, the label and labeling of the additive and of any feed additive supplement, feed additive concentrate, or feed additive premix prepared therefrom, shall contain, in addition to other information required by the Act, the following:

(1) The name of the additive.

(2) The maximum percentage of equivalent crude protein from the nonprotein nitrogen.

(3) Directions for use to provide not more than 20 percent of the additive in the total ration, and a prominent statement: "Warning—This feed should be used only in accordance with the directions furnished on the label."

§ 573.180 Anhydrous ammonia.

(a) The food additive anhydrous ammonia is applied directly to corn plant material and thoroughly blended prior to ensiling. It is used or intended for use as a source of nonprotein nitrogen in cattle feed in accordance with paragraphs (a)(1), (2), or (3) as follows:

(1)(i) The food additive anhydrous ammonia is applied as a component of an aqueous premix containing 16 to 17 percent ammonia, with molasses, minerals, and not less than 83 percent crude protein. The premix is a source of nonprotein nitrogen and minerals.

(ii) In addition to the requirements of paragraph (b) of this section, the labeling shall bear an expiration date of not more than 10 weeks after date of manufacture; a statement that additional protein should not be fed to lactating dairy cows producing less than

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32 pounds of milk per day nor beef cattle consuming less than 1 percent of body weight daily in shelled corn; and a warning not to use additional trace mineral supplementation with treated silage.

(2)(i) The food additive anhydrous ammonia is applied directly to corn plant material for use in dairy or beef cattle rations.

(ii) The anhydrous ammonia is applied at a rate not to exceed the equivalent of 0.35 percent of the corn plant material.

(iii) It is applied to corn plant material containing 30 to 35 percent dry matter.

(iv) It is applied so that 75 to 85 percent of the additive is liquid at ambient pressure.

(3)(i) The food additive anhydrous ammonia is applied after being diluted to a 15 to 30 percent aqueous ammonia solution (by weight).

(ii) The anhydrous ammonia solution is applied at a rate not to exceed anhydrous ammonia equivalent to 0.3 percent of the corn plant material.

(iii) It is applied to corn plant material containing 28 to 38 percent dry matter.

(iv) The silage treated with aqueous ammonia is to be fed to dairy cattle only.

(b) Its labeling shall bear, in addition to the other requirements of the Act, the name of the additive, the concentration of ammonia, the maximum percentage of equivalent crude protein from nonprotein nitrogen, and directions for use consistent with this section.

[44 FR 40284, July 10, 1979]

§ 573.200 Condensed animal protein hydrolysate.

(a) *Identity.* The condensed animal protein hydrolysate is produced from the meat byproducts scraped from cured (salted) hides taken from cattle slaughtered for food consumption. The meat byproduct is hydrolyzed with heat and phosphoric acid.

(b) *Specifications.* The additive shall conform to the following percent-by-weight specifications:

Moisture, not less than 45 percent nor more than 50 percent.

Protein, not less than 24 percent.
Salt (NaCl), not more than 15 percent.
Phosphorus, not less than 2.25 percent.

(c) *Uses.* It is used or intended for use as a source of animal protein, phosphorus, and salt (NaCl) as follows:

(1) In poultry and swine feed in an amount not to exceed 5 percent by weight of the feed.

(2) In feed concentrates for cattle in an amount not to exceed 10 percent by weight of the concentrate.

(d) *Labeling.* The label and labeling shall bear, in addition to the other information required by the Act:

(1) The name of the additive, condensed animal protein hydrolysate.

(2) Adequate directions for use including maximum quantities permitted for each species and a guaranteed analysis of the additive.

§ 573.220 Feed-grade biuret.

The food additive feed grade biuret may be safely used in ruminant feed in accordance with the following prescribed conditions:

(a) The food additive is the product resulting from the controlled pyrolysis of urea conforming to the following specifications:

	Percent
Biuret	55 minimum.
Urea	15 maximum.
Cyanic acid and biuret	30 maximum.
Mineral oil	0.5 maximum.
Total nitrogen (equivalent to 218.75 pct crude protein)	35 minimum.

(b) It is used in ruminant feeds as a source of nonprotein nitrogen.

(c) To assure safe use of the additive:

(i) The label and labeling of the additive and that of any feed additive supplement, feed additive concentrate, feed additive premix, or complete feed prepared therefrom shall contain, in addition to other information required by the Act, the following:

(i) The name of the additive.

(ii) The maximum percentage of equivalent crude protein from nonprotein nitrogen.

(iii) The statement "Do not feed to animals producing milk for human consumption."

(2) The label shall recommend that the diet be balanced to provide adequate nutrients when equivalent crude protein from all forms of nonprotein nitrogen exceed one-third of the total crude protein in the total daily ration.

§ 573.225 1,3-Butylene glycol.

The food additive 1,3-butylene glycol (1,3-butanediol) may be safely used in accordance with the following prescribed conditions:

(a) It complies with the specifications in § 173.220(a) of this chapter.

(b) It is intended for use in swine feed as a source of energy.

(c) It is to be thoroughly mixed into feed at levels not to exceed 9 percent of the dry matter of the total ration.

(d) 1,3-Butylene glycol should be mixed in feed with equipment adapted for the addition of liquids, and the feed should be mixed not less than 5 minutes after its addition.

[53 FR 40061, Oct. 13, 1988]

§ 573.240 Calcium periodate.

The food additive calcium periodate may be safely used in accordance with the following prescribed conditions:

(a) The additive is produced by reacting calcium iodate with calcium hydroxide or calcium oxide to form a substance consisting of not less than 60 percent by weight of penta calcium orthoperiodate containing 28 to 31 percent by weight of iodine.

(b) It is used or intended for use in salt for livestock as a source of iodine.

§ 573.260 Calcium silicate.

Calcium silicate, including synthetic calcium silicate, may be safely used as an anticaking agent in animal feed, provided that the amount of calcium silicate does not exceed 2 percent.

§ 573.280 Feed-grade calcium stearate.

Feed-grade calcium stearate may be safely used in an animal feed in accordance with the following prescribed conditions:

(a) Feed-grade calcium stearate is the calcium salt of a fatty acid mixture that is predominately stearic acid. Associated fatty acids, including palmitic acid and minor amounts of lauric, myristic, pentadecanoic, mar-

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garic, arachidic, and other fatty acids may be contained in the mixture, but such associated fatty acids in aggregate do not exceed 35 percent by weight of the mixture. The fatty acids may be derived from feed-grade fats or oils.

(b) The additive meets the following specifications:

(1) Unsaponifiable matter does not exceed 2 percent.

(2) It is free of chick-edema factor.

(c) The additive is manufactured so that in aqueous solution it is exposed for 1 hour or longer to temperature in excess of 180° F.

(d) It is used as an anticaking agent in animal feeds in accordance with good manufacturing practice.

§ 573.300 Choline xanthate.

Choline xanthate may be safely used as a component of animal feed as an added source of choline to supplement the diets of poultry, ruminants, and swine in accordance with good feeding practice.

§ 573.310 Crambe meal, heat toasted.

(a) The additive is the seed meal of *Crambe abyssinica* obtained after the removal of oil from the seed and hull. The oil may be removed by pre-press solvent extraction or by solvent extraction alone. The resulting seed meal is heat toasted.

(b) The additive conforms to the following percent-by-weight specifications: moisture, not more than 11 percent; oil, not more than 4 percent; crude protein, not less than 24 percent; crude fiber, not more than 26 percent; glucosinolate calculated as epi-progoitrin, not more than 4 percent; goitrin, not more than 0.1 percent; nitrile calculated as 1-cyano-2-hydroxy-3-butene, not more than 1.4 percent. At least 50 percent of the nitrogen shall be soluble in 0.5 M sodium chloride. Myrosinase enzyme activity shall be absent.

(c) The additive is used or intended for use in the feed of feedlot cattle as a source of protein in an amount not to exceed 4.2 percent of the total ration.

[46 FR 30082, June 5, 1981]

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§ 573.320 Diammonium phosphate.

The food additive diammonium phosphate may be safely used in ruminant feed in accordance with the following prescribed conditions:

(a) The food additive is the product resulting from the neutralization of feeding-phosphoric-acid or defluorinated wet-process phosphoric acid with anhydrous ammonia. It contains not less than 106.25 percent equivalent crude protein (nitrogen X 6.25) and 20 percent phosphorus. It contains not more than the following:

1 part fluorine to 100 parts phosphorus.

75 parts per million or arsenic (as As).

30 parts per million of heavy metals, as lead (Pb).

(b) It is used in ruminant feeds as a source of phosphorus and nitrogen in an amount that supplies not more than 2 percent of equivalent crude protein in the total daily ration.

(c) To assure safe use of the additive, the label and labeling of the additive and that of any feed additive supplement, feed additive concentrate, feed additive premix, or complete feed prepared therefrom shall contain, in addition to other information required by the Act, the following:

(1) The name of the additive.

(2) The maximum percentage of equivalent crude protein from the nonprotein nitrogen.

(3) If the feed additive premix, feed additive concentrate, or feed additive supplement contains more than 2 percent equivalent crude protein from diammonium phosphate, adequate directions for use and a prominent statement, "Warning—This feed should be used only in accordance with directions furnished on the label."

§ 573.340 Diatomaceous earth.

(a) *Identity*. The additive consists of siliceous skeletal material derived from various species of diatoms.

(b) *Specifications*. The additive shall conform to the following specifications:

Lead, not more than 15 parts per million.

Arsenic (as As), not more than 20 parts per million

Fluorine, not more than 600 parts per million.

(c) *Uses.* It is used or intended for use as an inert carrier or anticaking agent in animal feeds in an amount not to exceed 2 percent by weight of the total ration.

§ 573.360 Disodium EDTA.

The food additive disodium EDTA (disodium ethylenediaminetetraacetate) may be safely used in animal feeds, in accordance with the following prescribed conditions:

(a) The food additive contains a minimum of 99 percent disodium ethylenediaminetetraacetate dihydrate ($C_{10}H_{16}O_{16}N_4Na_2 \cdot 2H_2O$).

(b) It is used to solubilize trace minerals in aqueous solutions, which are then added to animal feeds.

(c) It is used or intended for use in an amount not to exceed 240 parts per million of the additive in finished feed.

(d) To assure safe use of the additive the label and labeling shall bear:

(1) The name of the additive; and

(2) Adequate mixing directions to ensure that the chelated trace-mineral mix is uniformly blended throughout the feed.

§ 573.380 Ethoxyquin in animal feeds.

Ethoxyquin (1,2-dihydro-6-ethoxy-2,2,4-trimethylquinoline) may be safely used in animal feeds, when incorporated therein in accordance with the following prescribed conditions.

(a) It is intended for use only: (1) As a chemical preservative for retarding oxidation of carotene, xanthophylls, and vitamins A and E in animal feed and fish food and, (2) as an aid in preventing the development of organic peroxides in canned pet food.

(b) The maximum quantity of the additive permitted to be used and to remain in or on the treated article shall not exceed 150 parts per million.

(c) To assure safe use of the additive, the label and labeling of the food additive container and that of any intermediate premixes prepared therefrom shall contain, in addition to other information required by the Act:

(1) The name of the additive, ethoxyquin.

(2) A statement of the concentration or strength contained therein.

(3) Adequate use directions to provide for a finished article with the proper concentration of the additive as provided in paragraph (b) of this section, whether or not intermediate premixes are to be used.

(d) The label of any animal feed containing the additive shall, in addition to the other information required by the Act, bear the statement "Ethoxyquin, a preservative" or "Ethoxyquin added to retard the oxidative destruction of carotene, xanthophylls, and vitamins A and E."

§ 573.400 Ethoxyquin in certain dehydrated forage crops.

Ethoxyquin (1,2-dihydro-6-ethoxy-2,2,4-trimethylquinoline) may be safely used in the dehydrated forage crops listed in paragraph (a) of this section when incorporated therein in accordance with the conditions prescribed in this section:

(a) It may be added to dehydrated forage prepared from:

Alfalfa	Medicago sativa.
Barley	Hordeum vulgare.
Clovers:	
Alsike clover	Trifolium hybridum.
Crimson clover	Trifolium incarnatum.
Red clover	Trifolium pratense.
White clover (including Ladino)	Trifolium repens.
White sweetclover	Melilotus alba.
Yellow sweetclover	Melilotus officinalis.
Coastal Bermudagrass	Cynodon dactylon.
Corn	Zea mays.
Fescue	Festuca sp.
Oats	Avena sativa.
Orchardgrass	Dactylis glomerata.
Reed canarygrass	Phalaris arundinacea.
Ryegrass (annual and perennial)	Elymus sp. and Lolium perenne.
Sorghums	Sorghum vulgare vars, feterita, shailu, kaoliang, broom-corn.
Sudan grass	Sorghum vulgare sudanense.
Wheat	Triticum aestivum.

or any mixture of such forage crops, for use only as an animal feed.

(b) Such additive is used only as a chemical preservative for the purpose of retarding oxidative destruction of naturally occurring carotenes and vitamin E in the forage crops.

(c) It is added to the dehydrated forage crops in an oil mixture containing only suitable animal or suitable vegetable oil, prior to grinding and mixing.

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(d) The maximum quantity of the additive permitted to be used and to remain in or on the dehydrated forage crop shall not exceed 150 parts per million.

(e) To assure the safe use of the additive, the label of the market package shall contain, in addition to other information required by the Act:

(1) The name of the additive as specified in this section.

(2) Directions for the incorporation of the additive in the forage crops, as specified in paragraph (c) of this section, with the directive that only suitable animal or suitable vegetable oils are to be used in the oil mix.

(f) The label of any dehydrated forage crops treated with the additive or the label of an animal-feed supplement containing such treated forage crops, shall, in addition to other information required by the Act, bear the following statements:

(1) "Ethoxyquin, a preservative," or "Ethoxyquin added to retard the oxidative destruction of carotene and vitamin E."

(2) The statement "For use in animal feed only."

§ 573.420 Ethyl cellulose.

The food additive ethyl cellulose may be safely used in animal feed in accordance with the following prescribed conditions:

(a) The food additive is a cellulose ether containing ethoxy (OC_2H_5) groups attached by an ether linkage and containing on an anhydrous basis not more than 2.6 ethoxy groups per anhydroglucose unit.

(b) It is used or intended for use as a binder or filler in dry vitamin preparations to be incorporated into animal feed.

§ 573.440 Ethylene dichloride.

The food additive ethylene dichloride may be safely used in the manufacture of animal feeds in accordance with the following prescribed conditions:

(a) It is used as a solvent in the extraction processing of animal byproducts for use in animal feeds.

(b) The maximum quantity of the additive permitted to remain in or on

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the extracted byproducts shall not exceed 300 parts per million.

(c) The extracted animal byproduct is added as a source of protein to a total ration at levels consistent with good feeding practices, but in no event at levels exceeding 13 percent of the total ration.

§ 573.450 Fermented ammoniated condensed whey.

(a) *Identity.* The product is produced by the *Lactobacillus bulgaricus* fermentation of whey with the addition of ammonia.

(b) *Specifications.* The product contains 35 to 55 percent crude protein and not more than 42 percent equivalent crude protein from nonprotein nitrogen sources.

(c) *Uses.* The product is used as a source of protein and nonprotein nitrogen for cattle.

(d) *Limitations.* (1) Store in a closed vented tank equipped for agitation. Agitate 5 minutes before using. Do not store at temperature above 110° F (43° C).

(2) The maximum level of use of fermented ammoniated condensed whey and equivalent crude protein from all other added forms of nonprotein nitrogen shall not exceed 30 percent of the dietary crude protein.

(3) The additive may be used as follows:

(i) Mixed with grain, roughage, or grain and roughage prior to feeding.

(ii) As a component of free-choice liquid feeds, used to supplement the diets of cattle fed other sources of nutrients, fermented ammoniated condensed whey shall not exceed 80 percent of the free-choice liquid feed.

(e) *Labeling.* The label shall bear, in addition to other information required by the act:

(1) The name of the additive.

(2) The maximum percentage of equivalent crude protein from nonprotein nitrogen.

(3) Adequate directions for use in accordance with the provisions in paragraph (d) of this section.

[43 FR 33708, July 1, 1978, as amended at 46 FR 49115, Oct. 6, 1981]

§ 573.460 Formaldehyde.

The food additive formaldehyde may be safely used in the manufacture of animal feeds in accordance with the following conditions:

(a) The additive is used, or intended for use, to improve the handling characteristics of animal fat in combination with certain oilseed meals by producing therefrom a dry, free-flowing product as follows:

(1) An aqueous blend of soybean and sunflower meals in a ratio of 3:1, respectively, is mixed with animal fat such that the oilseed meals and animal fat are in a ratio of 3:2. The feed ingredients are those defined by the "Official Publication" of the Association of American Feed Control Officials, Inc., 1976 ed., pages 86, 103, and 106.

(2) Formaldehyde (37 percent solution) is added to the mixture at a level of 4 percent of the dry matter weight of the oilseed meals and animal fat. This mixture, upon drying, contains not more than 1 percent formaldehyde and not more than 12 percent moisture.

(b) The dried mixture described in paragraph (a) of this section is used, or intended for use, as a component of dry, nonpelleted feeds for beef and nonlactating dairy cattle.

(c) To assure safe use of the additive, in addition to the other information required by the Act, the label and labeling of the dried mixture described in paragraph (a) of this section shall bear:

(1) The name of the additive.
(2) Adequate directions for use providing that feed as consumed is not to contain more than 25 percent of the mixture.

§ 573.480 Formic acid.

Formic acid may be safely used as a preservative in hay crop silage in an amount not to exceed 2.25 percent of the silage on a dry weight basis or 0.45 percent when direct-cut. The top foot of silage stored should not contain formic acid and silage should not be

fed to livestock within 4 weeks of treatment.

§ 573.500 Condensed, extracted glutamic acid fermentation product.

Condensed, extracted glutamic acid fermentation product may be safely used in animal feed under the following conditions:

(a) The additive is a concentrated mixture of the liquor remaining from the extraction of glutamic acid, combined with the cells of *Corynebacterium lilium* used to produce the glutamic acid.

(b) It is used or intended for use as follows:

(1) In poultry feed as a source of protein in an amount not to exceed 5 percent of the total ration.

(2) In cattle feed as a source of protein in an amount not to exceed 10 percent of the feed.

(c) In order to assure safe use, the label and labeling of the additive shall bear, in addition to the other information required by the Act, the following:

(1) The name of the additive.
(2) A statement of the concentration of the additive contained in any mixture.
(3) Adequate directions for use.

§ 573.520 Hemicellulose extract.

Hemicellulose extract may be safely used in animal feed when incorporated therein in accordance with the following conditions:

(a) The additive is produced from the aqueous extract obtained by the treatment of wood with water at elevated temperatures (325 degrees-535 degrees F) and pressure (80 to 900 pounds per square inch) and contains primarily pentose and hexose sugars.

(b) The additive may be used in a liquid or dry state with the liquid product containing not less than 55 percent carbohydrate and the dry product containing not less than 84 percent carbohydrate.

(c) The additive is used as a source of metabolizable energy in animal feed in accordance with good manufacturing and feeding practices.

[41 FR 38652, Sept. 10, 1976, as amended at 43 FR 11181, Mar. 17, 1978]

Copies may be obtained from: Ernest A. Pa. Jr., Treasurer, Division of Agricultural Chemistry, P.O. Box 16390-A, Baton Rouge, LA 70803.

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§ 573.530 Hydrogenated corn syrup.

(a) *Identity.* The product is produced by hydrogenation of corn syrup over a nickel catalyst.

(b) *Specifications.* The product contains 70 percent hydrogenated corn syrup and a maximum of 0.5 percent reducing sugars.

(c) *Uses.* The product is used as a humectant and plasticizer in preparation of soft-moist dog and cat foods.

(d) *Limitations.* The product is preferably stored in a closed, stainless steel or aluminum container. The level of use of the product shall not exceed 15 percent of the total weight of the pet food formulation.

(e) *Labeling.* The labeling shall bear, in addition to other information required by the Act:

(1) The name of the additive.

(2) Adequate directions for use in accordance with the provisions in paragraph (d) of this section.

[45 FR 22920, Apr. 4, 1980]

§ 573.540 Hydrolyzed leather meal.

(a) *Identity.* Hydrolyzed leather meal is produced from leather scraps that are treated with steam for not less than 33 minutes at a pressure of not less than 125 pounds per square inch.

(b) *Specifications.* The additive shall conform to the following percent-by-weight specifications:

Moisture, not less than 5 percent nor more than 10 percent.

Crude protein, not less than 60 percent.

Crude fat, not less than 5 percent.

Crude fiber, not more than 6 percent.

Chromium, not more than 2.75 percent.

(c) *Use.* It is used or intended for use as a source of protein in swine feeds in an amount not to exceed 1.0 percent by weight of the finished feed.

(d) *Labeling.* The labels and labeling shall bear, in addition to the other information required by the Act:

(1) The name of the additive, hydrolyzed leather meal.

(2) Adequate directions to provide finished feeds complying with paragraph (c) of this section.

§ 573.560 Iron ammonium citrate.

Iron ammonium citrate may be safely used in animal feed in accordance with the following prescribed conditions:

ance with the following prescribed conditions:

(a) The additive is the chemical green ferric ammonium citrate.

(b) The additive is used or intended for use as an anticaking agent in salt for animal consumption so that the level of iron ammonium citrate does not exceed 25 parts per million (0.0025 percent) in the finished salt.

(c) To assure safe use of the additive the label or labeling of the additive shall bear, in addition to the other information required by the Act:

(1) The name of the additive.

(2) Adequate directions to provide a final product that complies with the limitations prescribed in paragraph (b) of this section.

§ 573.580 Iron-choline citrate complex.

Iron-choline citrate complex made by reacting approximately equimolecular quantities of ferric hydroxide, choline, and citric acid may be safely used as a source of iron in animal feed.

§ 573.600 Lignin sulfonates.

Lignin sulfonates may be safely used in animal feeds in accordance with the following prescribed conditions:

(a) For the purpose of this section, the food additive is either one, or a combination of, the ammonium, calcium, magnesium, or sodium salts of the extract of spent sulfite liquor derived from the sulfite digestion of wood or of abaca (*Musa textilis*) or of sisal (*Agave sisalana*) in either a liquid form (moisture not to exceed 50 percent by weight) or dry form (moisture not to exceed 6 percent by weight).

(b) It is used or intended for use in an amount calculated on a dry weight basis, as follows:

(1) As a pelleting aid in the liquid or dry form in an amount not to exceed 4 percent of the finished pellets.

(2) As a binding aid in the liquid form in the flaking of feed grains in an amount not to exceed 4 percent of the flaked grain.

(3) As a surfactant in molasses used in feeds, as liquid lignin sulfonate, in an amount not to exceed 11 percent of the molasses.

(4) As a source of metabolizable energy, in the liquid or dry form, in an

amount not to exceed 4 percent of the finished feed.

§ 573.620 Menadione dimethylpyrimidinol bisulfite.

The food additive, menadione dimethylpyrimidinol bisulfite, may be safely used in accordance with the following conditions:

(a) The additive is the 2-hydroxy-4,6-dimethylpyrimidinol salt of menadione ($C_{17}H_{15}O_3N_2S$).

(b) The additive is used or intended for use as a nutritional supplement for the prevention of vitamin K deficiency as follows:

(1) In chicken and turkey feed at a level not to exceed 2 grams per ton of complete feed.

(2) In the feed of growing and finishing swine at a level not to exceed 10 grams per ton of feed.

(c) To assure safe use, the label and labeling of the additive shall bear adequate directions for use.

§ 573.640 Methyl esters of higher fatty acids.

The food additive methyl esters of higher fatty acids may be safely used in animal feeds in accordance with the following prescribed conditions:

(a) The food additive is manufactured by reaction of methyl alcohol with feed-grade fats or oils and consists of not less than 70 percent methyl esters of the following straight-chain monocarboxylic acids: Docosahexanoic acid, eicosapentanoic acid, linoleic acid, myristic acid, oleic acid, palmitic acid, palmitoleic acid, and stearic acid, and lesser amounts of the associated acid esters.

(b) The food additive meets the following specifications:

(1) Free methyl alcohol not to exceed 150 parts per million.

(2) Unsaponifiable matter not to exceed 2 percent.

(3) It is free of chick-edema factor or other factors toxic to chicks, as evidenced during the bioassay method for determining the chick-edema factor as prescribed in paragraph (4)(ii) of this section.

(4) For the purposes of this section:

(i) Unsaponifiable matter shall be determined by the method described

Section 28.081, "Unsaponifiable

Residue (20)—Official Final Action" of the "Official Methods of Analysis of the Association of Official Analytical Chemists," 13th Ed., 1980, p. 451, which is incorporated by reference. Copies are available from the Association of Official Analytical Chemists, P.O. Box 540, Benjamin Franklin Station, Washington, DC 20044, or available for inspection at the Office of the Federal Register, 1100 L St. NW., Washington, DC 20408.

(ii) The chick-edema factor bioassay method described under "28. Oils, Fats, and Waxes" in the *Journal of the Association of Official Agricultural Chemists*, Vol. 44, Page 146 (1961), or the method described under "Chick-Edema Factor—Bioassay Method (34)—Official Final Action" in §§ 28.113–28.117, "Official Methods of Analysis of the Association of Official Analytical Chemists," 12th Ed., 1975, pp. 509–511, which is incorporated by reference, shall be employed. (Copies of the methods are available from the Association of Official Analytical Chemists, P.O. Box 540, Benjamin Franklin Station, Washington, DC 20044, or available for inspection at the Office of the Federal Register, 1100 L St. NW., Washington, DC 20408.) The presence of chick-edema factor shall be determined by a comparison between the mean log of the pericardial fluid volumes of a test group and of a concurrent negative control group. The significance of the difference in pericardial fluid volumes between the test group and the negative control group is determined by calculating a "t" value according to the formula:

$$t = \frac{\bar{x}_1 - \bar{x}_2}{\sqrt{(s_1^2/n_1) + (s_2^2/n_2)}}$$

where:

$\bar{x}_1$ and $\bar{x}_2$ are the means of the logs of the pericardial fluid volumes of the test and control groups, respectively;

n_1 and n_2 are the number of chicks in the respective groups;

s_1^2 and s_2^2 are the variances of the test and control groups, respectively.

The variances are calculated as follows:

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$$s^2 = \frac{n(\sum x^2) - (\sum x)^2}{n(n-1)}$$

where:

$\sum x$ is the sum of the logs of the pericardial fluid volumes;

$\sum x^2$ is the sum of the squares of the logs of the pericardial fluid volumes for either the test t or control c group data.

The test sample is judged to contain chick-edema factor if the calculated " t " exceeds +1.3 and the mean log of the pericardial fluid volume obtained from the negative control group multiplied by 100 is less than 1.1461.

(iii) "Other factors toxic to chicks" referred to in paragraph (b)(3) of this section shall be determined during the course of the bioassay test described in paragraph (b)(4)(ii) of this section, on the basis of chick deaths or other abnormalities not attributable to chick-edema factor or to the experimental conditions of the test.

(c) It is used or intended for use as a supplementary source of fat for animal feed.

(d) To assure safe use of the additive, in addition to the other information required by the act:

(1) The label and labeling of the additive, and any feed additive supplement, feed additive concentrate, feed additive premix, or complete feed prepared therefrom shall bear:

(i) The name of the additive.

(ii) The designation "feed grade" in juxtaposition with the name and equally as prominent.

(2) The label or labeling of the additive and any feed additive supplement, feed additive concentrate, feed additive premix, or complete feed prepared therefrom shall bear adequate directions for use.

[41 FR 38652, Sept. 10, 1976, as amended at 47 FR 9397, Mar. 5, 1982]

§ 573.660 Methyl glucoside-coconut oil ester.

Methyl glucoside-coconut oil ester may be safely used in accordance with the following conditions:

(a) The additive meets the specifications prescribed in § 172.816 of this chapter.

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(b) It is used as a surfactant in molasses intended for use in animal feed at a level not to exceed 320 parts per million.

§ 573.680 Mineral oil.

Mineral oil may be safely used in animal feed, subject to the provisions of this section.

(a) Mineral oil, for the purpose of this section, is that complying with the definition and specifications contained in § 172.878 (a) and (b) or in § 178.3620(b)(1) (i) and (ii) of this chapter.

(b) It is used in animal feeds for the following purposes:

(1) To reduce dustiness of feeds or mineral supplements.

(2) To serve as a lubricant in the preparation of pellets, cubes, or blocks and to improve resistance to moisture of such pellets, cubes, or blocks.

(3) To prevent the segregation of trace minerals in mineralized salt.

(4) To serve as a diluent carrier in the manufacture of feed grade bluret in accordance with good manufacturing practice.

(5) For the removal of water from substances intended as ingredients of animal feed.

(c) The quantity of mineral oil used in animal feed shall not exceed 3.0 percent in mineral supplements, nor shall it exceed 0.06 percent of the total ration when present in feed or feed concentrates.

(Sec. 409, 72 Stat. 1784-1788 as amended (21 U.S.C. 348))

[41 FR 38652, Sept. 10, 1976, as amended at 47 FR 41106, Sept. 17, 1982]

§ 573.700 Sodium nitrite.

Sodium nitrite may be safely used in canned pet food containing meat and fish in accordance with the following prescribed conditions:

(a) It is used or intended for use alone as a preservative and color fixative in canned pet food containing fish, meat, and fish and meat byproducts so that the level of sodium nitrite does not exceed 20 parts per million.

(b) To assure safe use of the additive, in addition to the other information required by the act:

(1) The label of the additive shall bear:

(i) The name of the additive.
(ii) A statement of the concentration of the additive in any mixture.

(3) The label or labeling shall bear adequate directions to provide a final product that complies with the limitations prescribed in paragraph (a) of this section.

§ 573.720 Petrolatum.

Petrolatum may be safely used in or on animal feed, subject to the following prescribed conditions:

(a) Petrolatum complies with the specifications set forth in the U.S. Pharmacopeia XVI for white petrolatum or in The National Formulary XII for yellow petrolatum.

(b) Petrolatum meets the following ultraviolet absorbance limits when subjected to the analytical procedure described in § 172.886(b) of this chapter.

Ultraviolet absorbance per centimeter path length:

Millimicrons	Maximum
280 to 289.....	0.25
290 to 299.....	.20
300 to 359.....	.14
360 to 400.....	.04

(c) It is used in animal feed for the following purposes:

(1) To reduce dustiness of feeds or mineral supplements.

(2) To serve as a lubricant in the preparation of pellets, cubes, or blocks, and to improve resistance to moisture of such pellets, cubes, or blocks.

(d) The quantity of petrolatum present in animal feeds from the uses specified in paragraph (c) of this section shall not exceed 3 percent in mineral supplements nor shall it exceed .04 percent of the total ration when present in feed or feed concentrates.

(e) When used in combination with technical white mineral oil for the uses described in paragraph (c) of this section, the total quantity of combined petrolatum and technical white mineral oil shall not exceed the limits prescribed in paragraph (d) of this section.

(f) Petrolatum may contain any antioxidant permitted in food by regulations issued in accordance with section 409 of the act, in an amount not greater than that required to produce its intended effect.

§ 573.740 Odorless light petroleum hydrocarbons.

Odorless light petroleum hydrocarbons complying with § 172.884(a) and (b) of this chapter may be safely used in an amount not in excess of that required as a component of insecticide formulations used in compliance with regulations issued in this part.

§ 573.760 Poloxalene.

The food additive poloxalene may be safely used in accordance with the following prescribed conditions:

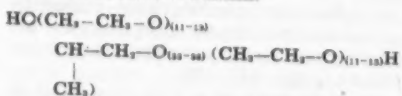
(a) The additive consists of polyoxypropylene-polyoxyethylene glycol non-ionic block polymer meeting the following specifications:

(1) Molecular weight range: 2,850-3,150.

(2) Hydroxyl number: 35.7-39.4.

(3) Cloud point (10 percent solution): 42° C-46° C.

(4) Structural formula:



(b) In feed as a surfactant for the flaking of feed grains when added to liquid grain conditioner in an amount not to exceed 1.0 percent of the conditioner. The conditioner is added to the feed at a rate of 1 quart per ton of feed.

(c) The label and labeling shall bear, in addition to the other information required by the Act:

(1) The name of the additive.

(2) Adequate directions and warnings for use.

§ 573.780 Polyethylene.

(a) *Identity.* Polyethylene consists of basic polymers manufactured by the catalytic polymerization of ethylene.

(b) *Specifications.* (1) For the purposes of this section, polyethylene shall meet the specifications in item 2.1 of § 121.2501(c) of this chapter.

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(2) The polyethylene is designed in a pellet form in a configuration presenting maximum angular surface having the following dimensions in centimeters:

$$0.9 \pm 0.1 \times 0.8 \pm 0.1 \times 1.2 \pm 0.1$$

(c) *Use.* It is used as a replacement for roughage in feedlot rations for finishing slaughter cattle.

(d) *Labeling.* The labels and labeling shall bear in addition to the other information required by the Act:

(1) The name of the additive "polyethylene roughage replacement."

(2) Adequate directions for use which shall provide for the administration of one-half pound of polyethylene pellets per head per day for 6 successive days. All natural roughage should be removed for a minimum of 12 hours prior to administration of polyethylene roughage replacement. Roughage replacement must be adequately mixed in the ration for uniform distribution.

§ 573.800 Polyethylene glycol (400) mono- and diolate.

(a) The food additive polyethylene glycol (400) mono- and diolate meets the following specifications: Saponification number, 80-88; acid number, 5.0 maximum; and average molecular weight range, 640-680.

(b) It is used as a processing aid in the production of animal feeds when present as a result of its addition to molasses in an amount not to exceed 250 parts per million of the molasses.

§ 573.820 Polyoxyethylene glycol (400) mono- and diolates.

The food additive polyoxyethylene glycol (400) mono- and diolates may be safely used as an emulsifier in calf-milk replacer formulations.

§ 573.840 Polysorbate 60.

The food additive polysorbate 60 (polyoxyethylene (20) sorbitan monostearate) may be safely used in animal feeds in accordance with the following prescribed conditions:

(a) It is used alone or in combination with sorbitan monostearate as an emulsifier in mineral premixes and dietary supplements for animal feeds.

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(b) It is used as an emulsifier in milk-replacer formulations for calves.

§ 573.860 Polysorbate 80.

The food additive polysorbate (polyoxyethylene (20) sorbitan mono-oleate) may be safely used as an emulsifier in milk-replacer formulations for calves.

§ 573.880 Normal propyl alcohol.

Normal propyl alcohol may be safely used in feeds and feed supplements for cattle as a source of metabolizable energy. It is incorporated in the feed or feed supplement in an amount which provides not more than 5 grams of the additive per head per day.

§ 573.900 Pyrophyllite.

Pyrophyllite (aluminum silicate monohydrate) may be safely used as the sole anticaking aid, blending agent, pelleting aid, or carrier in animal feed when incorporated therein in an amount not to exceed 2 percent in complete animal feed.

§ 573.914 Salts of volatile fatty acids.

(a) *Identity.* The food additive is a blend containing the ammonium calcium salt of isobutyric acid and the ammonium or calcium salts of a mixture of 5-carbon acids—isovaleric, methylbutyric, and *n*-valeric.

(b) *Specifications.* The additive contains ammonium or calcium salts of volatile fatty acids and shall conform to the following specifications:

(1) Ammonium salts:

Components	Amount
Ammonium salts of mixed 5-carbon acids (as identified in paragraph (a) of this section).	48 to 54 percent.
Ammonium salt of isobutyric acid.	22 to 26 percent.
Water.....	26 percent maximum.
Ammonia.....	0.3 percent maximum.
Arsenic.....	< 3 parts per million.
Heavy metals as lead.....	< 10 parts per million.

(2) Calcium salts:

Components	Amount
Calcium salts of mixed 5-carbon acids (as identified in paragraph (a) of this section).	58 to 72 percent.

Components	Amount
Calcium salt of isobutyric acid	26 to 34 percent.
Calcium hydroxide	3 percent maximum.
Water	14 percent maximum.
Arsenic	<3 parts per million.
Heavy metals as lead	<10 parts per million.

(c) *Use.* The additive is used or intended for use as a source of energy in dairy cattle feed.

(d) *Labeling.* The label and label of the additive in any feed, feed supplement, feed concentrate, feed premix, or liquid feed supplement prepared therefrom shall bear, in addition to other information required by the act, the following:

(1) The name of the additive.

(2) Adequate directions for use, including statements expressing maximum use levels. For ammonium salts of volatile fatty acids, the statements: "Not to exceed 160 grams per head per day thoroughly mixed in dairy cattle feed as a source of energy." For calcium salts of volatile fatty acids, the statement: "Not to exceed 135 grams per head per day thoroughly mixed in dairy cattle feed as a source of energy."

(Secs. 201(s), 409, 72 Stat. 1784-1788 as amended (21 U.S.C. 321(s), 348))

[40 FR 45125, Nov. 15, 1984; 50 FR 8606, Mar. 4, 1985]

§ 573.920 Selenium.

The food additive selenium may be safely used in accordance with the following prescribed conditions:

(a) The additive is used in animal feed as a nutrient in the form of sodium selenite or sodium selenate.

(b) It is added to feed as follows:

(1) In complete feed for chickens, swine, turkeys, sheep, cattle, and ducks at a level not to exceed 0.3 part per million.

(2) In feed supplements for limit feeding as follows:

(i) *Sheep:* At a level not to exceed an intake of 0.7 milligram per head per day.

(ii) *Beef cattle:* At a level not to exceed an intake of 3 milligrams per head per day.

(3) In salt-mineral mixtures for free-choice feeding as follows:

(i) *Sheep:* Up to 90 parts per million in a mixture for free-choice feeding at a rate not to exceed an intake of 0.7 milligram per head per day.

(ii) *Beef cattle:* Up to 120 parts per million in a mixture for free-choice feeding at a rate not to exceed an intake of 3 milligrams per head per day.

(c) The additive shall be incorporated into feed as follows:

(1) It shall be incorporated into each ton of complete feed by adding no less than 1 pound of a premix containing no more than 272.4 milligrams of added selenium per pound.

(2) It shall be incorporated into each ton of salt-mineral mixture for sheep or beef cattle from a premix containing no more than 4.5 grams of added selenium per pound.

(d) The premix manufacturer shall follow good manufacturing practices in the production of selenium premixes. Inventory, production, and distribution records must provide a complete and accurate history of product production. Production controls must assure products to be what they are purported and labeled. Production controls shall include analysis sufficient to adequately monitor quality.

(e) The label or labeling of any selenium premix shall bear adequate directions and cautions for use including this statement: "Caution: Follow label directions. The addition to feed of higher levels of this premix containing selenium is not permitted."

[52 FR 10888, Apr. 6, 1987; 52 FR 21001, June 4, 1987]

§ 573.940 Silicon dioxide.

The food additive silicon dioxide may be safely used in animal feed in accordance with the following conditions:

(a) The food additive is manufactured by vapor phase hydrolysis or by other means whereby the particle size is such as to accomplish the intended effect.

(b) It is used or intended for use in feed components as an anticaking agent, and/or grinding aid, as follows:

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Feed component	Limitations (percent)
BHT (butylated hydroxytoluene).....	2
Methionine hydroxy analog and its calcium salts.....	1
Piperazine, piperazine salts.....	0.6
Sodium propionate.....	1
Urea.....	1
Vitamins.....	3

(c) It is used in feed as an anticaking agent in an amount not to exceed that reasonably required to accomplish its intended effect and in no case in an amount to exceed 2 percent by weight of the finished feed.

§ 573.960 Sorbitan monostearate.

The food additive sorbitan monostearate may be safely used alone or in combination with polysorbate 60 as an emulsifier in mineral premixes and dietary supplements for animal feeds.

§ 573.980 Taurine.

The food additive taurine (2-aminoethanesulfonic acid) may be safely used in feed in accordance with the following prescribed conditions:

(a) It is used as a nutritional supplement in the feed of growing chickens.

(b) It is added to complete feeds so that the total taurine content does not exceed 0.054 percent of the feed.

(c) To assure safe use of the additive, the label and labeling shall bear in addition to the other information required by the Act:

(1) The name of the additive.

(2) The quantity of the additive contained therein.

(3) Adequate directions for use.

§ 573.1000 Verxite.

The food additive verxite may be safely used in animal feed in accordance with the following prescribed conditions:

(a) The additive is a magnesium-aluminum-iron silicate conforming to one of the following:

(1)(i) Verxite granules: The additive contains a minimum of 98 percent of hydrobiotite; it is thermally expanded and has a bulk density of from 5 to 9 pounds per cubic foot.

(ii) It is used or intended for use:

(a) In poultry feed at a level not to exceed 5 percent of the weight of the finished feed as a nonnutritive bulking

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agent for restricting calorie intake in pullet replacement feeds.

(b) As an anticaking or blending agent, pelleting aid, or nonnutritive carrier for the incorporation of nutrients in poultry, swine, dog, or ruminant feeds, in an amount not to exceed that necessary to accomplish its intended effect and in no case to exceed 1.5 percent of the dog feed or 5 percent of the final feed for other animals.

(2)(i) Verxite flakes: The additive contains a minimum of 98 percent hydrobiotite; it has a bulk density from 20 to 30 pounds per cubic foot.

(ii) It is used or intended for use as an anticaking or blending agent in ruminant feeds in an amount not to exceed that necessary to accomplish its intended effect and in no case to exceed 1 percent by weight of the final feed for ruminants.

(3)(i) Verxite grits: The additive contains a minimum of 80 percent of hydrobiotite; it has a bulk density from 40 to 50 pounds per cubic foot.

(ii) It is used or intended for use as partial roughage replacement in ruminant feeds in an amount not to exceed that necessary to accomplish its intended effect and in no case to exceed 1 percent by weight of the final feed.

(b) To assure safe use of the additive, the label of any feed additive supplement, feed additive concentrate, feed additive premix, or complete feed prepared therefrom shall bear, in addition to the other information required by the Act, the name of the additive (verxite granules, verxite flakes, or verxite grits), adequate directions for use, and, when the additive is present in excess of 1 percent, a statement of the quantity of the additive contained therein in the term "nonnutritive" in juxtaposition therewith.

§ 573.1010 Xanthan gum.

The food additive xanthan gum may be safely used in animal feed as follows:

(a) The food additive is xanthan gum as defined in § 172.695 of this chapter and meets all of the specifications thereof.

(b) It is used or intended for use as a stabilizer, emulsifier, thickener, stabilizer,

pending agent, or bodying agent in animal feed as follows:

(1) In calf milk replacers at a maximum use level of 0.1 percent, as fed.

(2) In liquid feed supplements for ruminant animals at a maximum use level of 0.25 percent (5 pounds per ton).

(c) To assure safe use of the additive:

(1) The label of its container shall bear, in addition to other information required by the act, the name of the additive.

(2) The label or labeling of the additive container shall bear adequate directions for use.

(Secs. 201(s), 409, 72 Stat. 1784-1788 as amended (21 U.S.C. 321(s), 348))

[49 FR 44630, Nov. 8, 1984]

§ 573.1020 Yellow prussiate of soda.

Yellow prussiate of soda (sodium ferrocyanide decahydrate: $\text{Na}_4\text{Fe}(\text{CN})_6 \cdot 10\text{H}_2\text{O}$) may be safely used as an anticaking agent in salt for animal consumption at a level not to exceed 13 parts per million. The additive contains a minimum of 99.0 percent by weight of sodium ferrocyanide decahydrate.

[41 FR 38657, Sept. 10, 1976; 41 FR 48100, Nov. 2, 1976]

PART 579—IRRADIATION IN THE PRODUCTION, PROCESSING, AND HANDLING OF ANIMAL FEED AND PET FOOD

Subpart A—General Provisions

Sec.
579.12 Incorporation of regulations in Part 179.

Subpart B—Radiation and Radiation Sources

579.22 Ionizing radiation for treatment of laboratory animal diets.

AUTHORITY: Secs. 201(s), 409, 72 Stat. 1784-1788 as amended (21 U.S.C. 321(s), 348); 21 CFR 5.10, 5.61.

Subpart A—General Provisions

579.12 Incorporation of regulations in Part 179.

Regulations providing for irradiation in the production, processing, and

handling of food in Part 179 of this chapter are incorporated in Subchapter E as applicable to use in the production, processing, handling, and labeling of animal feed and pet food, except where specifically provided for in this part.

[51 FR 5993, Feb. 19, 1986]

Subpart B—Radiation and Radiation Sources

579.22 Ionizing radiation for treatment of laboratory animal diets.

Ionizing radiation for treatment of complete diets for laboratory animals (mice, rats, and hamsters) may be safely used under the following conditions:

(a) *Energy sources.* Ionizing radiation is limited to:

(1) Gamma rays for sealed units of the radionuclides cobalt-60 or cesium-137.

(2) Electrons generated from machine sources at energy levels not to exceed 10 million electron volts.

(b) *Uses.* The ionizing radiation is used or intended for use in single treatment as follows:

Food for radiation	Limitations	Use
Bagged complete diets for laboratory animals (mice, rats, and hamsters).	Absorbed dose: Not to exceed 25 kiloGrays (2.5 megarads).	Microbial disinfection.

[51 FR 5993, Feb. 19, 1986; 51 FR 8315, Mar. 11, 1986]

PART 582—SUBSTANCES GENERALLY RECOGNIZED AS SAFE

Subpart A—General Provisions

Sec.

582.1 Substances that are generally recognized as safe.

582.10 Spices and other natural seasonings and flavorings.

582.20 Essential oils, oleoresins (solvent-free), and natural extractives (including distillates).

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Sec.

- 582.30 Natural substances used in conjunction with spices and other natural seasonings and flavorings.
- 582.40 Natural extractives (solvent-free) used in conjunction with spices, seasonings, and flavorings.
- 582.50 Certain other spices, seasonings, essential oils, oleoresins, and natural extracts.
- 582.60 Synthetic flavoring substances and adjuvants.
- 582.80 Trace minerals added to animal feeds.
- 582.99 Adjuvants for pesticide chemicals.

Subpart B—General Purpose Food Additives

- 582.1005 Acetic acid.
- 582.1009 Adipic acid.
- 582.1033 Citric acid.
- 582.1057 Hydrochloric acid.
- 582.1061 Lactic acid.
- 582.1069 Malic acid.
- 582.1073 Phosphoric acid.
- 582.1077 Potassium acid tartrate.
- 582.1087 Sodium acid pyrophosphate.
- 582.1091 Succinic acid.
- 582.1095 Sulfuric acid.
- 582.1099 Tartaric acid.
- 582.1125 Aluminum sulfate.
- 582.1127 Aluminum ammonium sulfate.
- 582.1129 Aluminum potassium sulfate.
- 582.1131 Aluminum sodium sulfate.
- 582.1135 Ammonium bicarbonate.
- 582.1137 Ammonium carbonate.
- 582.1139 Ammonium hydroxide.
- 582.1141 Ammonium phosphate.
- 582.1143 Ammonium sulfate.
- 582.1155 Bentonite.
- 582.1165 Butane.
- 582.1191 Calcium carbonate.
- 582.1193 Calcium chloride.
- 582.1195 Calcium citrate.
- 582.1199 Calcium gluconate.
- 582.1205 Calcium hydroxide.
- 582.1207 Calcium lactate.
- 582.1210 Calcium oxide.
- 582.1217 Calcium phosphate.
- 582.1235 Caramel.
- 582.1240 Carbon dioxide.
- 582.1275 Dextrins.
- 582.1320 Glycerin.
- 582.1324 Glyceryl monostearate.
- 582.1355 Helium.
- 582.1366 Hydrogen peroxide.
- 582.1400 Lecithin.
- 582.1425 Magnesium carbonate.
- 582.1428 Magnesium hydroxide.
- 582.1431 Magnesium oxide.
- 582.1480 Methylcellulose.
- 582.1500 Monoammonium glutamate.
- 582.1516 Monopotassium glutamate.
- 582.1540 Nitrogen.
- 582.1585 Papain.
- 582.1613 Potassium bicarbonate.

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Sec.

- 582.1619 Potassium carbonate.
- 582.1625 Potassium citrate.
- 582.1631 Potassium hydroxide.
- 582.1643 Potassium sulfate.
- 582.1655 Propane.
- 582.1666 Propylene glycol.
- 582.1685 Rennet.
- 582.1711 Silica aerogel.
- 582.1721 Sodium acetate.
- 582.1736 Sodium bicarbonate.
- 582.1742 Sodium carbonate.
- 582.1745 Sodium carboxymethylcellulose.
- 582.1748 Sodium caseinate.
- 582.1751 Sodium citrate.
- 582.1763 Sodium hydroxide.
- 582.1775 Sodium pectinate.
- 582.1778 Sodium phosphate.
- 582.1781 Sodium aluminum phosphate.
- 582.1792 Sodium sesquicarbonate.
- 582.1804 Sodium potassium tartrate.
- 582.1810 Sodium tripolyphosphate.
- 582.1901 Triacetin.
- 582.1973 Beeswax.
- 582.1975 Bleached beeswax.
- 582.1978 Carnauba wax.

Subpart C—Anticaking Agents

- 582.2122 Aluminum calcium silicate.
- 582.2227 Calcium silicate.
- 582.2437 Magnesium silicate.
- 582.2727 Sodium aluminosilicate.
- 582.2729 Hydrated sodium calcium aluminosilicate.
- 582.2906 Tricalcium silicate.

Subpart D—Chemical Preservatives

- 582.3013 Ascorbic acid.
- 582.3021 Benzoic acid.
- 582.3041 Erythorbic acid.
- 582.3081 Propionic acid.
- 582.3089 Sorbic acid.
- 582.3109 Thiodipropionic acid.
- 582.3149 Ascorbyl palmitate.
- 582.3169 Butylated hydroxyanisole.
- 582.3173 Butylated hydroxytoluene.
- 582.3189 Calcium ascorbate.
- 582.3221 Calcium propionate.
- 582.3225 Calcium sorbate.
- 582.3280 Dilauryl thiodipropionate.
- 582.3336 Gum guaiac.
- 582.3490 Methylparaben.
- 582.3616 Potassium bisulfite.
- 582.3637 Potassium metabisulfite.
- 582.3640 Potassium sorbate.
- 582.3660 Propyl gallate.
- 582.3670 Propylparaben.
- 582.3731 Sodium ascorbate.
- 582.3733 Sodium benzoate.
- 582.3739 Sodium bisulfite.
- 582.3766 Sodium metabisulfite.
- 582.3784 Sodium propionate.
- 582.3795 Sodium sorbate.
- 582.3798 Sodium sulfite.

Sec.
582.3845 Stannous chloride.
582.3862 Sulfur dioxide.
582.3890 Tocopherols.

Subpart E—Emulsifying Agents

582.4101 Diacetyl tartaric acid esters of mono- and diglycerides of edible fats or oils, or edible fat-forming fatty acids.
582.4905 Mono- and diglycerides of edible fats or oils, or edible fat-forming acids.
582.4521 Monosodium phosphate derivatives of mono- and diglycerides of edible fats or oils, or edible fat-forming fatty acids.
582.4666 Propylene glycol.

Subpart F—Nutrients and/or Dietary Supplements

582.5013 Ascorbic acid.
582.5017 Aspartic acid.
582.5040 Aminoacetic acid.
582.5065 Linoleic acid.
582.5118 Alanine.
582.5145 Arginine.
582.5159 Biotin.
582.5191 Calcium carbonate.
582.5195 Calcium citrate.
582.5201 Calcium glycerophosphate.
582.5210 Calcium oxide.
582.5212 Calcium pantothenate.
582.5217 Calcium phosphate.
582.5223 Calcium pyrophosphate.
582.5230 Calcium sulfate.
582.5245 Carotene.
582.5250 Choline bitartrate.
582.5252 Choline chloride.
582.5260 Copper gluconate.
582.5271 Cysteine.
582.5273 Cystine.
582.5301 Ferric phosphate.
582.5304 Ferric pyrophosphate.
582.5306 Ferric sodium pyrophosphate.
582.5308 Ferrous gluconate.
582.5311 Ferrous lactate.
582.5315 Ferrous sulfate.
582.5361 Histidine.
582.5370 Inositol.
582.5375 Iron reduced.
582.5381 Isoleucine.
582.5406 Leucine.
582.5411 Lysine.
582.5431 Magnesium oxide.
582.5434 Magnesium phosphate.
582.5443 Magnesium sulfate.
582.5446 Manganese chloride.
582.5449 Manganese citrate.
582.5452 Manganese gluconate.
582.5455 Manganese glycerophosphate.
582.5458 Manganese hypophosphite.
582.5461 Manganese sulfate.
582.5464 Manganous oxide.
582.5470 Mannitol.
582.5475 Methionine.

Sec.
582.5477 Methionine hydroxy analog and its calcium salts.
582.5530 Niacin.
582.5535 Niacinamide.
582.5580 D-Pantothenyl alcohol.
582.5590 Phenylalanine.
582.5622 Potassium chloride.
582.5628 Potassium glycerophosphate.
582.5634 Potassium iodide.
582.5650 Proline.
582.5676 Pyridoxine hydrochloride.
582.5695 Riboflavin.
582.5697 Riboflavin-5-phosphate.
582.5701 Serine.
582.5772 Sodium pantothenate.
582.5778 Sodium phosphate.
582.5835 Sorbitol.
582.5875 Thiamine hydrochloride.
582.5878 Thiamine mononitrate.
582.5881 Threonine.
582.5890 Tocopherols.
582.5892 α -Tocopherol acetate.
582.5915 Tryptophane.
582.5920 Tyrosine.
582.5925 Valine.
582.5930 Vitamin A.
582.5933 Vitamin A acetate.
582.5936 Vitamin A palmitate.
582.5945 Vitamin B₁₂.
582.5950 Vitamin D₃.
582.5953 Vitamin D₂.
582.5985 Zinc chloride.
582.5988 Zinc gluconate.
582.5991 Zinc oxide.
582.5994 Zinc stearate.
582.5997 Zinc sulfate.

Subpart G—Sequestrants

582.6033 Citric acid.
582.6085 Sodium acid phosphate.
582.6099 Tartaric acid.
582.6185 Calcium acetate.
582.6193 Calcium chloride.
582.6195 Calcium citrate.
582.6197 Calcium diacetate.
582.6199 Calcium gluconate.
582.6203 Calcium hexametaphosphate.
582.6215 Monobasic calcium phosphate.
582.6219 Calcium phytate.
582.6285 Dipotassium phosphate.
582.6290 Disodium phosphate.
582.6386 Isopropyl citrate.
582.6511 Monoisopropyl citrate.
582.6625 Potassium citrate.
582.6751 Sodium citrate.
582.6754 Sodium diacetate.
582.6757 Sodium gluconate.
582.6760 Sodium hexametaphosphate.
582.6769 Sodium metaphosphate.
582.6778 Sodium phosphate.
582.6787 Sodium pyrophosphate.
582.6789 Tetra sodium pyrophosphate.
582.6801 Sodium tartrate.
582.6804 Sodium potassium tartrate.

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Sec.	
582.6807	Sodium thiosulfate.
582.6810	Sodium tripolyphosphate.
582.6851	Stearyl citrate.

Subpart H—Stabilizers

582.7115	Agar-agar.
582.7133	Ammonium alginate.
582.7187	Calcium alginate.
582.7355	Chondrus extract.
582.7330	Gum arabic.
582.7333	Gum ghatti.
582.7339	Guar gum.
582.7343	Locust bean gum.
582.7349	Sterculia gum.
582.7351	Gum tragacanth.
582.7610	Potassium alginate.
582.7724	Sodium alginate.

AUTHORITY: Secs. 201(a), 409, 701, 52 Stat. 1055-1056 as amended, 72 Stat. 1784-1788 as amended (21 U.S.C. 321(a), 348, 371).

SOURCE: 41 FR 38657, Sept. 10, 1976, unless otherwise noted.

Subpart A—General Provisions

§ 582.1 Substances that are generally recognized as safe.

(a) It is impracticable to list all substances that are generally recognized as safe for their intended use. However, by way of illustration, the Commissioner regards such common food ingredients as salt, pepper, sugar, vinegar, baking powder, and monosodium glutamate as safe for their intended use. The lists in Subparts B through H of this part include additional substances that, when used for the purposes indicated, in accordance with good manufacturing or feeding practice, are regarded by the Commissioner as generally recognized as safe for such uses.

(b) For the purposes of this section, good manufacturing or feeding practice shall be defined to include the following restrictions:

(1) The quantity of a substance added to animal food does not exceed the amount reasonably required to accomplish its intended physical, nutri-

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tional, or other technical effect on food; and

(2) The quantity of a substance that becomes a component of animal food as a result of its use in the manufacturing, processing, or packaging of food, and which is not intended to accomplish any physical or other technical effect in the food itself, shall be reduced to the extent reasonably possible.

(3) The substance is of appropriate grade and is prepared and handled as a food ingredient. Upon request the Commissioner will offer an opinion based on specifications and intended use, as to whether or not a particular grade or lot of the substance is of suitable purity for use in food and would generally be regarded as safe for the purpose intended, by experts qualified to evaluate its safety.

(c) The inclusion of substances in the list of nutrients does not constitute a finding on the part of the Department that the substance is useful as a supplement to the diet for animals.

(d) Substances that are generally recognized as safe for their intended use within the meaning of section 409 of the Act are listed in Subparts B through H of this part. When the status of a substance has been reevaluated and affirmed as GRAS or deleted from Subparts B through H of this part, an appropriate explanation will be noted, e.g., "affirmed as GRAS," "food additive regulation," "interim food additive regulation," or "prohibited from use in food," with a reference to the appropriate new regulation. Such notation will apply only to the specific use covered by the review, e.g., direct animal food use and/or indirect animal food use and/or animal feed use and will not affect its status for other uses not specified in the referenced regulation, pending a specific review of such other uses.

§ 582.10 Spices and other natural seasonings and flavorings.

Spices and other natural seasonings and flavorings that are generally recognized as safe for their intended use, within the meaning of section 409 of the act, are as follows:

Common name	Botanical name of plant source
Alfalfa herb and seed	<i>Medicago sativa</i> L.
Alfalfa	<i>Pimenta officinalis</i> Lindl.
Amorite seed	<i>Hibiscus abelmoschus</i> L.
Angelica	<i>Angelica archangelica</i> L. or other spp. of <i>Angelica</i> .
Angelica root	Do.
Angelica seed	Do.
Angelica (cusparia bark)	<i>Galipea officinalis</i> Hancock.
Anise	<i>Pimpinella anisum</i> L.
Anise, star	<i>Illicium verum</i> Hook. f.
Balm (lemon balm)	<i>Melissa officinalis</i> L.
Basil, bush	<i>Ocimum minimum</i> L.
Basil, sweet	<i>Ocimum basilicum</i> L.
Bay	<i>Laurus nobilis</i> L.
Calendula	<i>Calendula officinalis</i> L.
Camomile (chamomile), English or Roman	<i>Anthemis nobilis</i> L.
Camomile (chamomile), German or Hungarian	<i>Matricaria chamomilla</i> L.
Capasa	<i>Capparis spinosa</i> L.
Capasaum	<i>Capsicum frutescens</i> L. or <i>Capsicum annuum</i> L.
Caraway	<i>Carum carvi</i> L.
Caraway, black (black cumin)	<i>Nigella sativa</i> L.
Cardamom (cardamom)	<i>Elettaria cardamomum</i> Maton.
Cassia, Chinese	<i>Cinnamomum cassia</i> Blume.
Cassia, Padang or Batavia	<i>Cinnamomum burmanni</i> Blume.
Cassia, Saigon	<i>Cinnamomum loureiri</i> Nees.
Cayenne pepper	<i>Capsicum frutescens</i> L. or <i>Capsicum annuum</i> L.
Celery seed	<i>Apium graveolens</i> L.
Chervil	<i>Anthriscus cerefolium</i> (L.) Hoffm.
Clove	<i>Allium schoenoprasum</i> L.
Clove, Ceylon	<i>Cinnamomum zeylanicum</i> Nees.
Clove, Chinese	<i>Cinnamomum cassia</i> Blume.
Clove, Saigon	<i>Cinnamomum loureiri</i> Nees.
Cilantro (cilantro)	<i>Salvia sclarea</i> L.
Clover	<i>Trifolium</i> spp.
Clove	<i>Eugenia caryophyllata</i> Thunb.
Coriander	<i>Coriandrum sativum</i> L.
Cumin (cumin)	<i>Cuminum cyminum</i> L.
Cumin, black (black caraway)	<i>Nigella sativa</i> L.
Do	<i>Anethum graveolens</i> L.
Star flowers	<i>Sambucus canadensis</i> L.
Fennel, common	<i>Foeniculum vulgare</i> Mill.
Fennel, sweet (finocchio, Florence fennel)	<i>Foeniculum vulgare</i> Mill. var. <i>duice</i> (DC.) Alex.
Fenugreek	<i>Trigonella foenum-graecum</i> L.
Galanga (galangal)	<i>Alpinia officinarum</i> Hance.
Garlic	<i>Allium sativum</i> L.
Ginseng	<i>Panax ginseng</i> spp.
Ginger	<i>Zingiber officinale</i> Rosc.
Glycyrrhiza	<i>Glycyrrhiza glabra</i> L. and other spp. of <i>Glycyrrhiza</i> .
Grains of paradise	<i>Amomum melegueta</i> Rosc.
Groundhallow (hoarhound)	<i>Marrubium vulgare</i> L.
Horseradish	<i>Armoracia lappathifolia</i> Glib.
Hyssop	<i>Hyssopus officinalis</i> L.
Lavender	<i>Lavandula officinalis</i> Chaix.
Licorice	<i>Glycyrrhiza glabra</i> L. and other spp. of <i>Glycyrrhiza</i> .
Loose flowers	<i>Tilia</i> spp.
Mace	<i>Myristica fragrans</i> Houtt.
Marigold, pot	<i>Calendula officinalis</i> L.
Marjoram, pot	<i>Majorana onites</i> (L.) Benth.
Marjoram, sweet	<i>Majorana hortensis</i> Moench.
Mustard, black or brown	<i>Brassica nigra</i> (L.) Koch.
Mustard, brown	<i>Brassica juncea</i> (L.) Coss.
Mustard, white or yellow	<i>Brassica hirta</i> Moench.
Nettle	<i>Myristica fragrans</i> Houtt.
Oregano (oregano, Mexican oregano, Mexican sage, origan)	<i>Lippia</i> spp.
Paprika	<i>Capsicum annuum</i> L.
Peppercorn	<i>Petroselinum crispum</i> (Mill.) Mansf.
Pepper, black	<i>Piper nigrum</i> L.
Pepper, cayenne	<i>Capsicum frutescens</i> L. or <i>Capsicum annuum</i> L.
Pepper, red	Do.
Pepper, white	<i>Piper nigrum</i> L.
Peppermint	<i>Mentha piperita</i> L.
Potato seed	<i>Papaver somniferum</i> L.
Pot marigold	<i>Calendula officinalis</i> L.
Pot marjoram	<i>Majorana onites</i> (L.) Benth.

Common name	Botanical name of plant source
Rosemary	<i>Roosmarinus officinalis</i> L.
Rue	<i>Ruta graveolens</i> L.
Saffron	<i>Crocus sativus</i> L.
Sage	<i>Salvia officinalis</i> L.
Sage, Greek	<i>Salvia triloba</i> L.
Savory, summer	<i>Satureia hortensis</i> L. (Satureja).
Savory, winter	<i>Satureia montana</i> L. (Satureja).
Sesame	<i>Sesamum indicum</i> L.
Spearmint	<i>Mentha spicata</i> L.
Star anise	<i>Illicium verum</i> Hook. f.
Tarragon	<i>Artemisia dracunculus</i> L.
Thyme	<i>Thymus vulgaris</i> L.
Thyme, wild or creeping	<i>Thymus serpyllum</i> L.
Turmeric	<i>Curcuma longa</i> L.
Vanilla	<i>Vanilla planifolia</i> Andr. or <i>Vanilla tahitensis</i> J. W. Moore
Zedoary	<i>Curcuma zedoaria</i> Rosc.

§ 582.20 Essential oils, oleoresins (solvent-free), and natural extractives (including distillates).

Essential oils, oleoresins (solvent-free), and natural extractives (including distillates) that are generally recognized as safe for their intended use, within the meaning of section 409 of the act, are as follows:

Common name	Botanical name of plant source
Alfalfa	<i>Medicago sativa</i> L.
Allspice	<i>Pimenta officinalis</i> Lindl.
Almond, bitter (free from prussic acid)	<i>Prunus amygdalus</i> Batsch, <i>Prunus armeniaca</i> L. or <i>Prunus persica</i> (L.) Batsch.
Ambrette (seed)	<i>Hibiscus moschatus</i> Moench.
Angelica root	<i>Angelica archangelica</i> L.
Angelica seed	Do.
Angelica stem	Do.
Angostura (cusparia bark)	<i>Galipea officinalis</i> Hancock.
Anise	<i>Pimpinella anisum</i> L.
Asafetida	<i>Ferula assa-foetida</i> L. and related spp. of <i>Ferula</i> .
Balm (lemon balm)	<i>Meissa officinalis</i> L.
Balsam of Peru	<i>Myroxylon peruviae</i> Klotzsch.
Basil	<i>Ocimum basilicum</i> L.
Bay leaves	<i>Laurus nobilis</i> L.
Bay (myrcia oil)	<i>Pimenta racemosa</i> (Mill.) J. W. Moore.
Bergamot (bergamot orange)	<i>Citrus aurantium</i> L. subsp. <i>bergamia</i> Wright et Arn.
Bitter almond (free from prussic acid)	<i>Prunus amygdalus</i> Batsch, <i>Prunus armeniaca</i> L. or <i>Prunus persica</i> (L.) Batsch.
Bois de rose	<i>Aniba roseodora</i> Ducke.
Cacao	<i>Theobroma cacao</i> L.
Camomile (chamomile) flowers, Hungarian	<i>Matricaria chamomilla</i> L.
Camomile (chamomile) flowers, Roman or English	<i>Anthemis nobilis</i> L.
Cananga	<i>Cananga odorata</i> Hook. f. and Thoms.
Capsicum	<i>Capsicum frutescens</i> L. and <i>Capsicum annuum</i> L.
Caraway	<i>Carum carvi</i> L.
Cardamom seed (cardamon)	<i>Elettaria cardamomum</i> Maion.
Carob bean	<i>Ceratonia siliqua</i> L.
Carrot	<i>Daucus carota</i> L.
Cascarilla bark	<i>Croton eluteria</i> Benn.
Cassia bark, Chinese	<i>Cinnamomum cassia</i> Blume.
Cassia bark, Padang or Batavia	<i>Cinnamomum burmanni</i> Blume.
Cassia bark, Saigon	<i>Cinnamomum loureiri</i> Nees.
Celery seed	<i>Apium graveolens</i> L.
Cherry, wild, bark	<i>Prunus serotina</i> Ehrh.
Chervil	<i>Anthriscus cerefolium</i> (L.) Hoffm.
Chicory	<i>Cichorium intybus</i> L.
Cinnamon bark, Ceylon	<i>Cinnamomum zeylanicum</i> Nees.
Cinnamon bark, Chinese	<i>Cinnamomum cassia</i> Blume.
Cinnamon bark, Saigon	<i>Cinnamomum loureiri</i> Nees.
Cinnamon leaf, Ceylon	<i>Cinnamomum zeylanicum</i> Nees.
Cinnamon leaf, Chinese	<i>Cinnamomum cassia</i> Blume.
Cinnamon leaf, Saigon	<i>Cinnamomum loureiri</i> Nees.

Common name	Botanical name of plant source
Citronella	<i>Cymbopogon nardus</i> Rendle.
Citrus peels	<i>Citrus</i> spp.
Clary (clary sage)	<i>Salvia sclarea</i> L.
Clove bud	<i>Eugenia caryophyllata</i> Thunb.
Clove leaf	Do.
Clove stem	Do.
Clover	<i>Trifolium</i> spp.
Coca (decocainized)	<i>Erythroxylum coca</i> Lam. and other spp. of <i>Erythroxylum</i> .
Coffee	<i>Coffea</i> spp.
Cola nut	<i>Cola acuminata</i> Schott and Endl., and other spp. of <i>Cola</i> .
Coriander	<i>Coriandrum sativum</i> L.
Corn silk	<i>Zea mays</i> L.
Cumin (cumin)	<i>Cuminum cyminum</i> L.
Curacao orange peel (orange, bitter peel)	<i>Citrus aurantium</i> L.
Cupressus bark	<i>Galipea officinalis</i> Hancock.
Dandelion	<i>Taraxacum officinale</i> Weber and T. <i>levigatum</i> DC.
Dandelion root	Do.
Oil	<i>Anethum graveolens</i> L.
Dog grass (quackgrass, triticum)	<i>Agropyron repens</i> (L.) Beauv.
Edible flowers	<i>Sambucus canadensis</i> L. and <i>S. nigra</i> L.
Eschschol (eschragol, esdragon, tarragon)	<i>Artemisia dracunculus</i> L.
Eschschol (tarragon)	Do.
Fennel, sweet	<i>Foeniculum vulgare</i> Mill.
Fragrant	<i>Trigonella foenum-graecum</i> L.
Galing (galingal)	<i>Alpinia officinarum</i> Hance.
Garlic	<i>Allium sativum</i> L.
Geranium	<i>Pelargonium</i> spp.
Geranium, East Indian	<i>Cymbopogon martinii</i> Stapf.
Geranium, rose	<i>Pelargonium graveolens</i> L'Her.
Ginger	<i>Zingiber officinale</i> Rosc.
Glycyrrhiza	<i>Glycyrrhiza glabra</i> L. and other spp. of <i>Glycyrrhiza</i> .
Glycyrrhizin, ammoniated	Do.
Guaiacum	<i>Citrus paradisi</i> Macf.
Guava	<i>Psidium</i> spp.
Hickory bark	<i>Carya</i> spp.
Hound (hoarhound)	<i>Marrubium vulgare</i> L.
Hops	<i>Humulus lupulus</i> L.
Horehound	<i>Monarda punctata</i> L.
Hyssop	<i>Hyssopus officinalis</i> L.
Immortelle	<i>Helichrysum augustifolium</i> DC.
Jasmine	<i>Jasminum officinale</i> L. and other spp. of <i>Jasminum</i> .
Juniper (berries)	<i>Juniperus communis</i> L.
Cola nut	<i>Cola acuminata</i> Schott and Endl., and other spp. of <i>Cola</i> .
Lavender	<i>Laurus nobilis</i> L.
Lavender, spike	<i>Laurus</i> spp.
Lavandin	<i>Lavandula officinalis</i> Chaix.
	<i>Lavandula latifolia</i> Vill.
	Hybrids between <i>Lavandula officinalis</i> Chaix and <i>Lavandula latifolia</i> Vill.
Lemon	<i>Citrus limon</i> (L.) Burm. f.
Lemon balm (see balm)	
Lemon grass	<i>Cymbopogon citratus</i> DC. and <i>Cymbopogon flexuosus</i> Stapf.
Lemon peel	<i>Citrus limon</i> (L.) Burm. f.
Licorice	<i>Glycyrrhiza glabra</i> L. and other spp. of <i>Glycyrrhiza</i> .
Lime	<i>Citrus aurantifolia</i> Swingle.
Linden flowers	<i>Tilia</i> spp.
Liquorice	<i>Ceratonia siliqua</i> L.
Lupulin	<i>Humulus lupulus</i> L.
Mace	<i>Myristica fragrans</i> Houtt.
Malt (extract)	<i>Hordeum vulgare</i> L., or other grains.
Mandarin	<i>Citrus reticulata</i> Blanco.
Marjoram, sweet	<i>Majorana hortensis</i> Moench.
Mate 1	<i>Ilex paraguariensis</i> St. Hil.
Melissa (see balm)	
Menthol	<i>Mentha</i> spp.
Menthyl acetate	Do.
Melissae (extract)	<i>Saccharum officinarum</i> L.
Mustard	<i>Brassica</i> spp.
Narange	<i>Citrus paradisi</i> Macf.
Narol, bigarade	<i>Citrus aurantium</i> L.
Narog	<i>Myristica fragrans</i> Houtt.
Onion	<i>Allium cepa</i> L.
Orange, bitter, flowers	<i>Citrus aurantium</i> L.

Common name	Botanical name of plant source
Orange, bitter, peel	Do.
Orange leaf	<i>Citrus sinensis</i> (L.) Osbeck.
Orange, sweet	Do.
Orange, sweet, flowers	Do.
Orange, sweet, peel	Do.
Origanum	<i>Origanum</i> spp.
Palmarosa	<i>Cymbopogon martini</i> Stapf.
Paprika	<i>Capaicum annuum</i> L.
Parsley	<i>Petroselinum crispum</i> (Mill.) Mansf.
Pepper, black	<i>Piper nigrum</i> L.
Pepper, white	<i>Piper nigrum</i> L.
Peppermint	<i>Mentha piperita</i> L.
Peruvian balsam	<i>Myroxylon peraeae</i> Klotzsch.
Petitgrain	<i>Citrus aurantium</i> L.
Petitgrain lemon	<i>Citrus limon</i> (L.) Burm. f.
Petitgrain mandarin or tangerine	<i>Citrus reticulata</i> Blanco.
Pimenta	<i>Pimenta officinalis</i> Lindl.
Pimenta leaf	<i>Pimenta officinalis</i> Lindl.
Pipsissewa leaves	<i>Chimaphila umbellata</i> Nutt.
Pomegranate	<i>Punica granatum</i> L.
Prickly ash bark	<i>Xanthoxylum</i> (or <i>Zanthoxylum</i>) <i>Americanum</i> Mill. or <i>Xanthoxylum clava-herculis</i> L.
Rose absolute	<i>Rosa alba</i> L., <i>Rosa centifolia</i> L., <i>Rosa damascena</i> Mill., <i>R. gallica</i> L., and vars. of these spp.
Rose (otto of roses, attar of roses)	Do.
Rose buds	Do.
Rose flowers	Do.
Rose fruit (hips)	Do.
Rose geranium	<i>Pelargonium graveolens</i> L'Her.
Rose leaves	<i>Rosa</i> spp.
Rosemary	<i>Rosmarinus officinalis</i> L.
Rue	<i>Ruta graveolens</i> L.
Saffron	<i>Crocus sativus</i> L.
Sage	<i>Salvia officinalis</i> L.
Sage, Greek	<i>Salvia triloba</i> L.
Sage, Spanish	<i>Salvia lavandulaefolia</i> Vahl.
St. John's bread	<i>Cerastium siliqua</i> L.
Savory, summer	<i>Satureia hortensis</i> L.
Savory, winter	<i>Satureia montana</i> L.
Schinus molle	<i>Schinus molle</i> L.
Sloe berries (blackthorn berries)	<i>Prunus spinosa</i> L.
Spearmint	<i>Mentha spicata</i> L.
Spike lavender	<i>Lavandula latifolia</i> Vill.
Tamarind	<i>Tamarindus indica</i> L.
Tangerine	<i>Citrus reticulata</i> Blanco.
Tannic acid	Nutgalls of <i>Quercus infectoria</i> Oliver and related spp. <i>Quercus</i> . Also in many other plants.
Tarragon	<i>Artemisia dracunculoides</i> L.
Tea	<i>Thea sinensis</i> L.
Thyme	<i>Thymus vulgaris</i> L. and <i>Thymus zygis</i> var. <i>gracilis</i> Boiss.
Thyme, white	Do.
Thyme, wild or creeping	<i>Thymus serpyllum</i> L.
Triticum (see dog grass).	
Tuberose	<i>Polianthes tuberosa</i> L.
Turmeric	<i>Curcuma longa</i> L.
Vanilla	<i>Vanilla planifolia</i> Andr. or <i>Vanilla tahitensis</i> J. W. Moore
Violet flowers	<i>Viola odorata</i> L.
Violet leaves	Do.
Violet leaves absolute	Do.
Wild cherry bark	<i>Prunus serotina</i> Ehrh.
Ylang-ylang	<i>Cananga odorata</i> Hook. f. and Thoms.
Zedoary bark	<i>Curcuma zedoaria</i> Rosc.

§ 582.30 Natural substances used in conjunction with spices and other natural seasonings and flavorings.

Natural substances used in conjunction with spices and other natural seasonings and flavorings that are generally recognized as safe for their intended use within the meaning of section 409 of the act, are as follows:

Common name	Botanical name of plant source
Algae, brown (kelp).....	<i>Laminaria</i> spp. and <i>Nereocystis</i> spp.
Algae, red.....	<i>Porphyra</i> spp. and <i>Rhodomenia palmata</i> (L.) Grev.
Dulse.....	<i>Rhodomenia palmata</i> (L.)

§ 582.40 Natural extractives (solvent-free) used in conjunction with spices, seasonings, and flavorings.

Natural extractives (solvent-free) used in conjunction with spices, seasonings, and flavorings that are generally recognized as safe for their intended use, within the meaning of section 409 of the act, are as follows:

Common name	Botanical name of plant source
Algae, brown.....	<i>Laminaria</i> spp. and <i>Nereocystis</i> spp.
Algae, red.....	<i>Porphyra</i> spp. and <i>Rhodomenia palmata</i> (L.) Grev.
Apricot kernel (persic oil).....	<i>Prunus armeniaca</i> L.
Dulse.....	<i>Rhodomenia palmata</i> (L.) Grev.
Kelp (see algae, brown).....	
Peach kernel (persic oil).....	<i>Prunus persica</i> Sieb. et Zucc.
Peanut stearine.....	<i>Arachis hypogaea</i> L.
Persic oil (see apricot kernel and peach kernel).....	
Quince seed.....	<i>Cydonia oblonga</i> Miller.

§ 582.50 Certain other spices, seasonings, essential oils, oleoresins, and natural extracts.

Certain other spices, seasonings, essential oils, oleoresins, and natural extracts that are generally recognized as safe for their intended use, within the meaning of section 409 of the act, are as follows:

Common name	Derivation
Ambergris.....	<i>Physeter macrocephalus</i> L.
Castoreum.....	Castor fiber L. and <i>C. canadensis</i> Kuhl.
Civet (zibeth, zibot, zibetum).....	Civet cats, <i>Viverra civetta</i> Schreber and <i>Viverra zibetha</i> Schreber.
Cognac oil, white and green.....	<i>Ethyl oenanthane</i> , so-called.
Musk (Tonquin musk).....	Musk deer, <i>Moschus moschiferus</i> L.

§ 582.60 Synthetic flavoring substances and adjuvants.

Synthetic flavoring substances and adjuvants that are generally recognized as safe for their intended use, within the meaning of section 409 of the act, are as follows:

Acetaldehyde (ethanal).
 Acetoin (acetyl methylcarbinol).
 Aconitic acid (equisetic acid, citridic acid, achilleic acid).
 Anethole (parapropenyl anisole).
 Benzaldehyde (benzoic aldehyde).
N-Butyric acid (butanoic acid).
d- or *l*-Carvone (carvol).
 Cinnamaldehyde (cinnamic aldehyde).
 Citral (2,6-dimethyloctadien-2,6-*di*-8, geranial, neral).
 Decanal (*N*-decylaldehyde, capraldehyde, capric aldehyde, caprinaldehyde, aldehyde C-10).

Diacetyl (2,3-butanedione). Ethyl acetate.
 Ethyl butyrate.
 3-Methyl-3-phenyl glycidic acid ethyl ester (ethyl-methyl-phenyl-glycidate, so-called strawberry aldehyde, C-16 aldehyde).
 Ethyl vanillin.
 Eugenol.
 Geraniol (3,7-dimethyl-2,6 and 3,6-octadien-1-ol).
 Geranyl acetate (geraniol acetate).
 Glycerol (glyceryl) tributyrate (tributyrin, butyrin).
 Limonene (*d*-, *l*-, and *dl*-).
 Linalool (linalol, 3,7-dimethyl-1,6-octadien-3-ol).
 Linalyl acetate (bergamol).
 Malic acid.
 Methyl anthranilate (methyl-2-aminobenzoate).
 Piperonal (3,4-methylenedioxy-benzaldehyde, heliotropin).
 Vanillin.

§ 582.80

§ 582.80 Trace minerals added to animal feeds.

These substances added to animal feeds as nutritional dietary supplements are generally recognized as safe when added at levels consistent with good feeding practice.¹

Element	Source compounds
Cobalt.....	Cobalt acetate. Cobalt carbonate. Cobalt chloride. Cobalt oxide. Cobalt sulfate.
Copper.....	Copper carbonate. Copper chloride. Copper gluconate. Copper hydroxide. Copper orthophosphate. Copper oxide. Copper pyrophosphate. Copper sulfate.
Iodine.....	Calcium iodate. Calcium iodobenzenate. Cuprous iodide. 3,5-Diodosalicylic acid. Ethylenediamine dihydroiodide. Potassium iodate. Potassium iodide. Sodium iodate. Sodium iodide. Thymol iodide.
Iron.....	Iron ammonium citrate. Iron carbonate. Iron chloride. Iron gluconate. Iron oxide. Iron phosphate. Iron pyrophosphate. Iron sulfate. Reduced iron.
Manganese.....	Manganese acetate. Manganese carbonate. Manganese citrate (soluble). Manganese chloride. Manganese gluconate. Manganese orthophosphate. Manganese phosphate (dibasic). Manganese sulfate. Manganous oxide.
Zinc.....	Zinc acetate. Zinc carbonate. Zinc chloride. Zinc oxide. Zinc sulfate.

§ 582.99 Adjuvants for pesticide chemicals.

Adjuvants, identified and used in accordance with 40 CFR 180.1001(c) and (d), which are added to pesticide use dilutions by a grower or applicator prior to application to the raw agricultural commodity, are exempt from the

¹ All substances listed may be in anhydrous or hydrated form.

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requirement of tolerances under section 409 of the act.

(Sec. 409, 72 Stat. 1785; 21 U.S.C. 348)

Subpart B—General Purpose Food Additives

§ 582.1005 Acetic acid.

(a) *Product.* Acetic acid.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1009 Adipic acid.

(a) *Product.* Adipic acid.

(b) [Reserved]

(c) *Limitations, restrictions, or explanation.* This substance is generally recognized as safe when used as a buffer and neutralizing agent in accordance with good manufacturing or feeding practice.

§ 582.1033 Citric acid.

(a) *Product.* Citric acid.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1057 Hydrochloric acid.

(a) *Product.* Hydrochloric acid.

(b) [Reserved]

(c) *Limitations, restrictions, or explanation.* This substance is generally recognized as safe when used as a buffer and neutralizing agent in accordance with good manufacturing or feeding practice.

§ 582.1061 Lactic acid.

(a) *Product.* Lactic acid.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1069 Malic acid.

(a) *Product.* Malic acid.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1073 Phosphoric acid.

(a) *Product.* Phosphoric acid.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1077 Potassium acid tartrate.

(a) *Product.* Potassium acid tartrate.
(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1087 Sodium acid pyrophosphate.

(a) *Product.* Sodium acid pyrophosphate.
(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1091 Succinic acid.

(a) *Product.* Succinic acid.
(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1095 Sulfuric acid.

(a) *Product.* Sulfuric acid.
(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1099 Tartaric acid.

(a) *Product.* Tartaric acid.
(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1125 Aluminum sulfate.

(a) *Product.* Aluminum sulfate.
(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1127 Aluminum ammonium sulfate.

(a) *Product.* Aluminum ammonium sulfate.
(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1129 Aluminum potassium sulfate.

(a) *Product.* Aluminum potassium sulfate.
(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1131 Aluminum sodium sulfate.

(a) *Product.* Aluminum sodium sulfate.
(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1135 Ammonium bicarbonate.

(a) *Product.* Ammonium bicarbonate.
(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1137 Ammonium carbonate.

(a) *Product.* Ammonium carbonate.
(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1139 Ammonium hydroxide.

(a) *Product.* Ammonium hydroxide.
(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1141 Ammonium phosphate.

(a) *Product.* Ammonium phosphate (mono- and dibasic).
(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1143 Ammonium sulfate.

(a) *Product.* Ammonium sulfate.
(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1155 Bentonite.

(a) *Product.* Bentonite.
(b) *Conditions of use.* This substance is generally recognized as safe when

§ 582.1165

used in accordance with good manufacturing or feeding practice.

§ 582.1165 Butane.

(a) *Product.* Butane.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1191 Calcium carbonate.

(a) *Product.* Calcium carbonate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1193 Calcium chloride.

(a) *Product.* Calcium chloride.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1195 Calcium citrate.

(a) *Product.* Calcium citrate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1199 Calcium gluconate.

(a) *Product.* Calcium gluconate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1205 Calcium hydroxide.

(a) *Product.* Calcium hydroxide.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1207 Calcium lactate.

(a) *Product.* Calcium lactate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1210 Calcium oxide.

(a) *Product.* Calcium oxide.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

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§ 582.1217 Calcium phosphate.

(a) *Product.* Calcium phosphate (mono-, di-, and tribasic).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1235 Caramel.

(a) *Product.* Caramel.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1240 Carbon dioxide.

(a) *Product.* Carbon dioxide.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1275 Dextrins.

(a) *Product.* Dextrins of average molecular weight below 100,000.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1320 Glycerin.

(a) *Product.* Glycerin.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1324 Glyceryl monostearate.

(a) *Product.* Glyceryl monostearate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1355 Helium.

(a) *Product.* Helium.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1366 Hydrogen peroxide.

(a) *Product.* Hydrogen peroxide.

(b) [Reserved]

(c) *Limitations, restrictions, or planation.* This substance is generally recognized as safe when used

bleaching agent in accordance with good manufacturing or feeding practice.

§ 582.1400 Lecithin.

(a) *Product.* Lecithin.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1425 Magnesium carbonate.

(a) *Product.* Magnesium carbonate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1428 Magnesium hydroxide.

(a) *Product.* Magnesium hydroxide.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1431 Magnesium oxide.

(a) *Product.* Magnesium oxide.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1486 Methylcellulose.

(a) *Product.* U.S.P. methylcellulose, except that the methoxy content shall not be less than 27.5 percent and not more than 31.5 percent on a dry-weight basis.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1500 Monoammonium glutamate.

(a) *Product.* Monoammonium glutamate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1516 Monopotassium glutamate.

(a) *Product.* Monopotassium glutamate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1540 Nitrogen.

(a) *Product.* Nitrogen.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1585 Papain.

(a) *Product.* Papain.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1613 Potassium bicarbonate.

(a) *Product.* Potassium bicarbonate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1619 Potassium carbonate.

(a) *Product.* Potassium carbonate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1625 Potassium citrate.

(a) *Product.* Potassium citrate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1631 Potassium hydroxide.

(a) *Product.* Potassium hydroxide.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1643 Potassium sulfate.

(a) *Product.* Potassium sulfate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1655 Propane.

(a) *Product.* Propane.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1666

§ 582.1666 Propylene glycol.

(a) *Product.* Propylene glycol.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1685 Rennet.

(a) *Product.* Rennet (rennin).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1711 Silica aerogel.

(a) *Product.* Silica aerogel as a finely powdered microcellular silica foam having a minimum silica content of 89.5 percent.

(b) [Reserved]

(c) *Limitations, restrictions, or explanation.* This substance is generally recognized as safe when used as a component of antifoaming agents in accordance with good manufacturing or feeding practice.

§ 582.1721 Sodium acetate.

(a) *Product.* Sodium acetate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1736 Sodium bicarbonate.

(a) *Product.* Sodium bicarbonate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1742 Sodium carbonate.

(a) *Product.* Sodium carbonate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1745 Sodium carboxymethylcellulose.

(a) *Product.* Sodium carboxymethylcellulose is the sodium salt of carboxymethylcellulose not less than 99.5 percent on a dry-weight basis, with maximum substitution of 0.95 carboxymethyl groups per anhydroglucose unit, and with a minimum viscosity of

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25 centipoises for 2 percent by weight aqueous solution at 25° C.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1748 Sodium caseinate.

(a) *Product.* Sodium caseinate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1751 Sodium citrate.

(a) *Product.* Sodium citrate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1763 Sodium hydroxide.

(a) *Product.* Sodium hydroxide.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1775 Sodium pectinate.

(a) *Product.* Sodium pectinate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1778 Sodium phosphate.

(a) *Product.* Sodium phosphate (mono-, di-, and tribasic).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1781 Sodium aluminum phosphate.

(a) *Product.* Sodium aluminum phosphate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1792 Sodium sesquicarbonate.

(a) *Product.* Sodium sesquicarbonate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1804 Sodium potassium tartrate.

(a) *Product.* Sodium potassium tartrate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1810 Sodium tripolyphosphate.

(a) *Product.* Sodium tripolyphosphate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1901 Triacetin.

(a) *Product.* Triacetin (glyceryl triacetate).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1973 Beeswax.

(a) *Product.* Beeswax (yellow wax).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1975 Bleached beeswax.

(a) *Product.* Bleached beeswax (white wax).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.1978 Carnauba wax.

(a) *Product.* Carnauba wax.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

Subpart C—Anticaking Agents

§ 582.2122 Aluminum calcium silicate.

(a) *Product.* Aluminum calcium silicate.

(b) *Tolerance.* 2 percent.

(c) *Limitations, restrictions, or explanation.* This substance is generally recognized as safe when used in table salt in accordance with good manufacturing or feeding practice.

§ 582.2227 Calcium silicate.

(a) *Product.* Calcium silicate.

(b) *Tolerance.* 2 percent and 5 percent.

(c) *Limitations, restrictions, or explanation.* This substance is generally recognized as safe when used at levels not exceeding 2 percent in table salt and 5 percent in baking powder in accordance with good manufacturing or feeding practice.

§ 582.2437 Magnesium silicate.

(a) *Product.* Magnesium silicate.

(b) *Tolerance.* 2 percent.

(c) *Limitations, restrictions, or explanation.* This substance is generally recognized as safe when used in table salt in accordance with good manufacturing or feeding practice.

§ 582.2727 Sodium aluminosilicate.

(a) *Product.* Sodium aluminosilicate (sodium silicoaluminate).

(b) *Tolerance.* This substance is generally recognized as safe for use at a level not exceeding 2 percent in accordance with good manufacturing or feeding practice.

§ 582.2729 Hydrated sodium calcium aluminosilicate.

(a) *Product.* Hydrated sodium calcium aluminosilicate (sodium calcium silicoaluminate).

(b) *Tolerance.* This substance is generally recognized as safe for use at a level not exceeding 2 percent in accordance with good manufacturing or feeding practice.

§ 582.2906 Tricalcium silicate.

(a) *Product.* Tricalcium silicate.

(b) *Tolerance.* 2 percent.

(c) *Limitations, restrictions, or explanation.* This substance is generally recognized as safe when used in table salt in accordance with good manufacturing or feeding practice.

Subpart D—Chemical Preservatives

§ 582.3013 Ascorbic acid.

(a) *Product.* Ascorbic acid.

(b) *Conditions of use.* This substance is generally recognized as safe when

§ 582.3021

used in accordance with good manufacturing or feeding practice.

§ 582.3021 Benzoic acid.

(a) *Product.* Benzoic acid.

(b) *Tolerance.* This substance is generally recognized as safe for use at a level not exceeding 0.1 percent in accordance with good manufacturing or feeding practice.

§ 582.3041 Erythorbic acid.

(a) *Product.* Erythorbic acid.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.3081 Propionic acid.

(a) *Product.* Propionic acid.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.3089 Sorbic acid.

(a) *Product.* Sorbic acid.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.3109 Thiodipropionic acid.

(a) *Product.* Thiodipropionic acid.

(b) *Tolerance.* This substance is generally recognized as safe for use in food when the total content of antioxidants is not over 0.02 percent of fat or oil content including essential (volatile) oil content of the food, provided the substance is used in accordance with good manufacturing or feeding practice.

§ 582.3149 Ascorbyl palmitate.

(a) *Product.* Ascorbyl palmitate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.3169 Butylated hydroxyanisole.

(a) *Product.* Butylated hydroxyanisole.

(b) *Tolerance.* This substance is generally recognized as safe for use in food when the total content of antioxidants is not over 0.02 percent of fat or oil content, including essential

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(volatile) oil content of food provided the substance is used in accordance with good manufacturing or feeding practice.

§ 582.3173 Butylated hydroxytoluene.

(a) *Product.* Butylated hydroxytoluene.

(b) *Tolerance.* This substance is generally recognized as safe for use in food when the total content of antioxidants is not over 0.02 percent of fat or oil content, including essential (volatile) oil content of food provided the substance is used in accordance with good manufacturing or feeding practice.

§ 582.3189 Calcium ascorbate.

(a) *Product.* Calcium ascorbate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.3221 Calcium propionate.

(a) *Product.* Calcium propionate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.3225 Calcium sorbate.

(a) *Product.* Calcium sorbate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.3280 Dilauryl thiodipropionate.

(a) *Product.* Dilauryl thiodipropionate.

(b) *Tolerance.* This substance is generally recognized as safe for use in food when the total content of antioxidants is not over 0.02 percent of fat or oil content, including essential (volatile) oil content of the food, provided the substance is used in accordance with good manufacturing or feeding practice.

§ 582.3336 Gum guaiac.

(a) *Product.* Gum guaiac.

(b) *Tolerance.* 0.1 percent (equivalent antioxidant activity 0.01 percent).

(c) *Limitations, restrictions, or explanation.* This substance is generally

recognized as safe when used in edible fats or oils in accordance with good manufacturing or feeding practice.

§ 582.3490 Methylparaben.

(a) *Product.* Methylparaben (methyl p-hydroxybenzoate).

(b) *Tolerance.* This substance is generally recognized as safe for use at a level not exceeding 0.1 percent in accordance with good manufacturing or feeding practice.

§ 582.3616 Potassium bisulfite.

(a) *Product.* Potassium bisulfite.

(b) [Reserved]

(c) *Limitations, restrictions, or explanation.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice, except that it is not used in meats or in food recognized as source of vitamin B₁.

§ 582.3637 Potassium metabisulfite.

(a) *Product.* Potassium metabisulfite.

(b) [Reserved]

(c) *Limitations, restrictions, or explanation.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice, except that it is not used in meats or in food recognized as source of vitamin B₁.

§ 582.3640 Potassium sorbate.

(a) *Product.* Potassium sorbate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.3660 Propyl gallate.

(a) *Product.* Propyl gallate.

(b) *Tolerance.* This substance is generally recognized as safe for use in food when the total content of antioxidants is not over 0.02 percent of fat or oil content, including essential (volatile) oil content of the food, provided the substance is used in accordance with good manufacturing or feeding practice.

§ 582.3670 Propylparaben.

(a) *Product.* Propylparaben (propyl p-hydroxybenzoate).

(b) *Tolerance.* This substance is generally recognized as safe for use at a level not exceeding 0.1 percent in accordance with good manufacturing or feeding practice.

§ 582.3731 Sodium ascorbate.

(a) *Product.* Sodium ascorbate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.3733 Sodium benzoate.

(a) *Product.* Sodium benzoate.

(b) *Tolerance.* This substance is generally recognized as safe for use at a level not exceeding 0.1 percent in accordance with good manufacturing or feeding practice.

§ 582.3739 Sodium bisulfite.

(a) *Product.* Sodium bisulfite.

(b) [Reserved]

(c) *Limitations, restrictions, or explanation.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice, except that it is not used in meats or in food recognized as source of vitamin B₁.

§ 582.3766 Sodium metabisulfite.

(a) *Product.* Sodium metabisulfite.

(b) [Reserved]

(c) *Limitations, restrictions, or explanation.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice, except that it is not used in meats or in food recognized as source of vitamin B₁.

§ 582.3784 Sodium propionate.

(a) *Product.* Sodium propionate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.3795 Sodium sorbate.

(a) *Product.* Sodium sorbate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.3798

§ 582.3798 Sodium sulfite.

(a) *Product.* Sodium sulfite.

(b) [Reserved]

(c) *Limitations, restrictions, or explanation.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice, except that it is not used in meats or in food recognized as source of vitamin B₁.

§ 582.3845 Stannous chloride.

(a) *Product.* Stannous chloride.

(b) *Tolerance.* This substance is generally recognized as safe for use at a level not exceeding 0.0015 percent calculated as tin in accordance with good manufacturing or feeding practice.

§ 582.3862 Sulfur dioxide.

(a) *Product.* Sulfur dioxide.

(b) [Reserved]

(c) *Limitations, restrictions, or explanation.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice, except that it is not used in meats or in food recognized as source of vitamin B₁.

§ 582.3890 Tocopherols.

(a) *Product.* Tocopherols.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

Subpart E—Emulsifying Agents

§ 582.4101 Diacetyl tartaric acid esters of mono- and diglycerides of edible fats or oils, or edible fat-forming fatty acids.

(a) *Product.* Diacetyl tartaric acid esters of mono- and diglycerides of edible fats or oils, or edible fat-forming fatty acids.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.4505 Mono- and diglycerides of edible fats or oils, or edible fat-forming acids.

(a) *Product.* Mono- and diglycerides of edible fats or oils, or edible fat-forming acids.

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(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.4521 Monosodium phosphate derivatives of mono- and diglycerides of edible fats or oils, or edible fat-forming fatty acids.

(a) *Product.* Monosodium phosphate derivatives of mono- and diglycerides of edible fats or oils, or edible fat-forming fatty acids.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.4666 Propylene glycol.

(a) *Product.* Propylene glycol.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

Subpart F—Nutrients and/or Dietary Supplements¹

§ 582.5013 Ascorbic acid.

(a) *Product.* Ascorbic acid.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5017 Aspartic acid.

(a) *Product.* Aspartic acid (L- and DL-forms).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5049 Aminoacetic acid.

(a) *Product.* Glycine (aminoacetic acid).

(b) [Reserved]

(c) *Limitations, restrictions, or explanation.* This substance is generally recognized as safe when used in animal feeds in accordance with good manufacturing or feeding practice.

¹ Amino acids listed in this subpart may be free hydrochloride salt, hydrated, or anhydrous form, where applicable.

§ 582.5065 Linoleic acid.

(a) *Product.* Linoleic acid prepared from edible fats and oils and free from chick-edema factor.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5118 Alanine.

(a) *Product.* Alanine (L- and DL-forms).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5145 Arginine.

(a) *Product.* Arginine (L- and DL-forms).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5159 Biotin.

(a) *Product.* Biotin.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5191 Calcium carbonate.

(a) *Product.* Calcium carbonate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5195 Calcium citrate.

(a) *Product.* Calcium citrate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5201 Calcium glycerophosphate.

(a) *Product.* Calcium glycerophosphate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5210 Calcium oxide.

(a) *Product.* Calcium oxide.

(b) *Conditions of use.* This substance is generally recognized as safe when

used in accordance with good manufacturing or feeding practice.

§ 582.5212 Calcium pantothenate.

(a) *Product.* Calcium pantothenate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5217 Calcium phosphate.

(a) *Product.* Calcium phosphate (mono-, di-, and tribasic).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5223 Calcium pyrophosphate.

(a) *Product.* Calcium pyrophosphate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5230 Calcium sulfate.

(a) *Product.* Calcium sulfate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5245 Carotene.

(a) *Product.* Carotene.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5250 Choline bitartrate.

(a) *Product.* Choline bitartrate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5252 Choline chloride.

(a) *Product.* Choline chloride.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5260 Copper gluconate.

(a) *Product.* Copper gluconate.

(b) *Tolerance.* This substance is generally recognized as safe for use at a level not exceeding 0.005 percent in ac-

§ 582.5271

cordance with good manufacturing or feeding practice.

§ 582.5271 Cysteine.

(a) *Product.* Cysteine (L-forms).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5273 Cystine.

(a) *Product.* Cystine (L- and DL-forms).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5301 Ferric phosphate.

(a) *Product.* Ferric phosphate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5304 Ferric pyrophosphate.

(a) *Product.* Ferric pyrophosphate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5306 Ferric sodium pyrophosphate.

(a) *Product.* Ferric sodium pyrophosphate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5308 Ferrous gluconate.

(a) *Product.* Ferrous gluconate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5311 Ferrous lactate.

(a) *Product.* Ferrous lactate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5315 Ferrous sulfate.

(a) *Product.* Ferrous sulfate.

(b) *Conditions of use.* This substance is generally recognized as safe when

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used in accordance with good manufacturing or feeding practice.

§ 582.5361 Histidine.

(a) *Product.* Histidine (L- and DL-forms).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5370 Inositol.

(a) *Product.* Inositol.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5375 Iron reduced.

(a) *Product.* Iron reduced.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5381 Isoleucine.

(a) *Product.* Isoleucine (L- and DL-forms).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5406 Leucine.

(a) *Product.* Leucine (L- and DL-forms).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5411 Lysine.

(a) *Product.* Lysine (L- and DL-forms).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5431 Magnesium oxide.

(a) *Product.* Magnesium oxide.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5434 Magnesium phosphate.

(a) *Product.* Magnesium phosphate (di- and tribasic).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5443 Magnesium sulfate.

(a) *Product.* Magnesium sulfate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5446 Manganese chloride.

(a) *Product.* Manganese chloride.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5449 Manganese citrate.

(a) *Product.* Manganese citrate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5452 Manganese gluconate.

(a) *Product.* Manganese gluconate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5455 Manganese glycerophosphate.

(a) *Product.* Manganese glycerophosphate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5458 Manganese hypophosphite.

(a) *Product.* Manganese hypophosphite.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5461 Manganese sulfate.

(a) *Product.* Manganese sulfate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5464 Manganous oxide.

(a) *Product.* Manganous oxide.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5470 Mannitol.

(a) *Product.* Mannitol.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5475 Methionine.

(a) *Product.* Methionine.

(b) [Reserved]

(c) *Limitations, restrictions, or explanation.* This substance is generally recognized as safe when used in animal feeds in accordance with good manufacturing or feeding practice.

§ 582.5477 Methionine hydroxy analog and its calcium salts.

(a) *Product.* Methionine hydroxy analog and its calcium salts.

(b) [Reserved]

(c) *Limitations, restrictions, or explanation.* This substance is generally recognized as safe when used in animal feeds in accordance with good manufacturing or feeding practice.

§ 582.5530 Niacin.

(a) *Product.* Niacin.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5535 Niacinamide.

(a) *Product.* Niacinamide.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5580 D-Pantothenyl alcohol.

(a) *Product.* D-Pantothenyl alcohol.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5590

§ 582.5590 Phenylalanine.

(a) *Product.* Phenylalanine (L- and DL-forms).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5622 Potassium chloride.

(a) *Product.* Potassium chloride.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5628 Potassium glycerophosphate.

(a) *Product.* Potassium glycerophosphate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5634 Potassium iodide.

(a) *Product.* Potassium iodide.

(b) *Tolerance.* 0.01 percent.

(c) *Limitations, restrictions, or explanation.* This substance is generally recognized as safe when used in table salt as a source of dietary iodine in accordance with good manufacturing or feeding practice.

§ 582.5650 Proline.

(a) *Product.* Proline (L- and DL-forms).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5676 Pyridoxine hydrochloride.

(a) *Product.* Pyridoxine hydrochloride.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5695 Riboflavin.

(a) *Product.* Riboflavin.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5697 Riboflavin-5-phosphate.

(a) *Product.* Riboflavin-5-phosphate.

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(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5701 Serine.

(a) *Product.* Serine (L- and DL-forms).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5772 Sodium pantothenate.

(a) *Product.* Sodium pantothenate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5778 Sodium phosphate.

(a) *Product.* Sodium phosphate (mono-, di-, and tribasic).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5835 Sorbitol.

(a) *Product.* Sorbitol.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5875 Thiamine hydrochloride.

(a) *Product.* Thiamine hydrochloride.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5878 Thiamine mononitrate.

(a) *Product.* Thiamine mononitrate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5881 Threonine.

(a) *Product.* Threonine (L- and DL-forms).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5890 Tocopherols.

- (a) *Product.* Tocopherols.
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5892 α -Tocopherol acetate.

- (a) *Product.* α -Tocopherol acetate.
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5915 Tryptophane.

- (a) *Product.* Tryptophane (L- and DL-forms).
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5920 Tyrosine.

- (a) *Product.* Tyrosine (L- and DL-forms).
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5925 Valine.

- (a) *Product.* Valine (L- and DL-forms).
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5930 Vitamin A.

- (a) *Product.* Vitamin A.
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5933 Vitamin A acetate.

- (a) *Product.* Vitamin A acetate.
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5936 Vitamin A palmitate.

- (a) *Product.* Vitamin A palmitate.
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5945 Vitamin B₁₂.

- (a) *Product.* Vitamin B₁₂.
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5950 Vitamin D₃.

- (a) *Product.* Vitamin D₃.
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5953 Vitamin D₂.

- (a) *Product.* Vitamin D₂.
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5985 Zinc chloride.

- (a) *Product.* Zinc chloride.
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5988 Zinc gluconate.

- (a) *Product.* Zinc gluconate.
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5991 Zinc oxide.

- (a) *Product.* Zinc oxide.
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5994 Zinc stearate.

- (a) *Product.* Zinc stearate prepared from stearic acid free from chick-edema factor.
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.5997 Zinc sulfate.

- (a) *Product.* Zinc sulfate.
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

Subpart G—Sequestrants²

§ 582.6033 Citric acid.

(a) *Product.* Citric acid.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.6085 Sodium acid phosphate.

(a) *Product.* Sodium acid phosphate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.6099 Tartaric acid.

(a) *Product.* Tartaric acid.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.6185 Calcium acetate.

(a) *Product.* Calcium acetate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.6193 Calcium chloride.

(a) *Product.* Calcium chloride.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.6195 Calcium citrate.

(a) *Product.* Calcium citrate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.6197 Calcium diacetate.

(a) *Product.* Calcium diacetate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.6199 Calcium gluconate.

(a) *Product.* Calcium gluconate.

²For the purpose of this subpart, no attempt has been made to designate those sequestrants that may also function as chemical preservatives.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.6203 Calcium hexametaphosphate.

(a) *Product.* Calcium hexametaphosphate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.6215 Monobasic calcium phosphate.

(a) *Product.* Monobasic calcium phosphate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.6219 Calcium phytate.

(a) *Product.* Calcium phytate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.6285 Dipotassium phosphate.

(a) *Product.* Dipotassium phosphate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.6290 Disodium phosphate.

(a) *Product.* Disodium phosphate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.6386 Isopropyl citrate.

(a) *Product.* Isopropyl citrate.

(b) *Tolerance.* This substance is generally recognized as safe for use at a level not exceeding 0.02 percent in accordance with good manufacturing or feeding practice.

§ 582.6511 Monoisopropyl citrate.

(a) *Product.* Monoisopropyl citrate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.6625 Potassium citrate.

- (a) *Product.* Potassium citrate.
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

[41 FR 38657, Sept. 10, 1976. Redesignated at 42 FR 14091, Mar. 15, 1977]

§ 582.6751 Sodium citrate.

- (a) *Product.* Sodium citrate.
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

[41 FR 38657, Sept. 10, 1976. Redesignated at 42 FR 14091, Mar. 15, 1977]

§ 582.6754 Sodium diacetate.

- (a) *Product.* Sodium diacetate.
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.6757 Sodium gluconate.

- (a) *Product.* Sodium gluconate.
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.6760 Sodium hexametaphosphate.

- (a) *Product.* Sodium hexametaphosphate.
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.6769 Sodium metaphosphate.

- (a) *Product.* Sodium metaphosphate.
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.6778 Sodium phosphate.

- (a) *Product.* Sodium phosphate (mono-, di-, and tribasic).
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.6787 Sodium pyrophosphate.

- (a) *Product.* Sodium pyrophosphate.

- (b) *Condition of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.6789 Tetra sodium pyrophosphate.

- (a) *Product.* Tetra sodium pyrophosphate.
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.6801 Sodium tartrate.

- (a) *Product.* Sodium tartrate.
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.6804 Sodium potassium tartrate.

- (a) *Product.* Sodium potassium tartrate.
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.6807 Sodium thiosulfate.

- (a) *Product.* Sodium thiosulfate.
- (b) *Tolerance.* 0.1 percent.
- (c) *Limitations, restrictions, or explanation.* This substance is generally recognized as safe when used in salt in accordance with good manufacturing or feeding practice.

§ 582.6810 Sodium tripolyphosphate.

- (a) *Product.* Sodium tripolyphosphate.
- (b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.6851 Stearyl citrate.

- (a) *Product.* Stearyl citrate.
- (b) *Tolerance.* This substance is generally recognized as safe for use at a level not exceeding 0.15 percent in accordance with good manufacturing or feeding practice.

Subpart H—Stabilizers

§ 582.7115 Agar-agar.

- (a) *Product.* Agar-agar.

§ 582.7133

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.7133 Ammonium alginate.

(a) *Product.* Ammonium alginate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.7187 Calcium alginate.

(a) *Product.* Calcium alginate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.7255 Chondrus extract.

(a) *Product.* Chondrus extract (carrageenin).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.7330 Gum arabic.

(a) *Product.* Acacia (gum arabic).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.7333 Gum ghatti.

(a) *Product.* Gum ghatti.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.7339 Guar gum.

(a) *Product.* Guar gum.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.7343 Locust bean gum.

(a) *Product.* Locust (carob) bean gum.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

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§ 582.7349 Sterculia gum.

(a) *Product.* Sterculia gum (karaya gum).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.7351 Gum tragacanth.

(a) *Product.* Tragacanth (gum tragacanth).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.7610 Potassium alginate.

(a) *Product.* Potassium alginate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

§ 582.7724 Sodium alginate.

(a) *Product.* Sodium alginate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

PART 584—FOOD SUBSTANCES AFFIRMED AS GENERALLY RECOGNIZED AS SAFE IN FEED AND DRINKING WATER OF ANIMALS

Subpart A—[Reserved]

Subpart B—Listing of Specific Substances Affirmed as GRAS

§ 584.200 Ethyl alcohol containing ethyl acetate.

The feed additive ethyl alcohol containing ethyl acetate meets the requirement of 27 CFR 212.45, being not less than 92.5 percent ethyl alcohol, each 100 gallons having had added the equivalent of 4.25 gallons of 100 percent ethyl acetate. It is used in accordance with good feeding practices in ruminant feed supplements as a source of added energy.

(Secs. 201(s), 409, 701(a), 52 Stat. 1055, 72 Stat. 1784-1788 as amended (21 U.S.C. 321(s), 348, 371(a)))

[46 FR 52333, Oct. 27, 1981]

**PART 589—SUBSTANCES PROHIBITED
FROM USE IN ANIMAL FOOD OR
FEED**

AUTHORITY: Secs. 201(s), 402, 409, 701(a),
82 Stat. 1046-1047 as amended, 1055, 72
Stat. 1784-1788 as amended (21 U.S.C.
321(s), 342, 348, 371(a)).

Subpart A—General Provisions

**§ 589.1 Substances prohibited from use in
animal food or feed.**

(a) The substances listed in this part have been prohibited from use in animal food or feed by the Food and Drug Administration because of a determination that they present a potential risk to the public health or have not been shown by adequate scientific data to be safe for use in such food or feed. Use of any of these substances in violation of this part causes the animal food or feed involved to be adulterated and in violation of the Act.

(b) This part includes only a partial list of substances prohibited from use in animal food or feed; it is for easy reference purposes and is not a complete list of substances that may not lawfully be used in such animal food or feed. No substance may be used in animal food or feed unless it meets all applicable requirements of the Act.

(c) The Food and Drug Administration either on its own initiative or on behalf of any interested person who has submitted a petition, may publish a proposal to establish, amend, or repeal a regulation under this part on the basis of new scientific evaluation or information. Any such petition shall include an adequate scientific basis to support the petition, shall be the form set forth in § 571.1 of this chapter, and will be published in the *FEDERAL REGISTER* for comment if it contains reasonable ground.

[45 FR 28319, Apr. 29, 1980]

PARTS 590—599—[RESERVED]

FINDING AIDS

of CFR titles, subtitles, chapters, subchapters and parts and an alphabetical list of agencies publishing in the CFR are included in the CFR Index and Finding Aids volume to the Code of Federal Regulations which is published separately and revised annually.

Material Approved for Incorporation by Reference
List of CFR Titles and Chapters
Alphabetical List of Agencies Appearing in the CFR
Designation Tables
of CFR Sections Affected

Material Approved for Incorporation by Reference

The Director of the Federal Register has approved under 5 U.S.C. 552(a) and 1 R Part 51 the incorporation by reference of the following publications. This contains only those incorporations by reference effective as of the revision of this volume. Incorporations by reference found within a regulation are effective upon the effective date of that regulation. For more information on incorporation by reference, see the preliminary pages of this volume.

CFR CHAPTER I (PARTS 500 TO 599)

FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES

21 CFR

Academic Press, Inc.

111 Fifth Ave., New York, NY 10003

method published in "Methods in Hormone Research," New York, 558.710(b)

Academic Press, Volume II, p. 286 (1962).

Association of Official Analytical Chemists

P.O. Box 540, Benjamin Franklin Station, Washington, DC 20044

Official Methods of Analysis, 13th Ed., 1980.

20.2320:

573.640(b)(4)(i) and (ii)

NOTE: The following materials are available through the Food and Drug Administration at the addresses indicated.

Bureau of Foods, Food and Drug Administration

100 C St. SW., Washington, DC 20204

Journal of the Association of Official Analytical Chemists:

Oils, Fats, and Waxes" Vol. 44(1) 146 (1961). 573.640(b)(4)(ii)

Right Method of E. J. Emborg, G. H. Cass and J. M. Curtis, published 556.250(b)

"Endocrinology", Vol. 63, p. 806 (1958).

Permits Management Branch (HFA-305), Food and Drug Administration

800 Fishers Lane, Room 4-82, Rockville, MD 20857

Determination of Factor Content in Tylosin by High Performance 520.2640; 522.2640n;

Liquid Chromatography.

522.2640b;
524.2640; 558.625;
558.630

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At 40 FR 13802, March 27, 1975, as amended at 41 FR 9149, Mar. 3, 1976; 41 FR 10886, Mar. 15, 1976, the animal drug regulations and the animal drug provisions in regulations formerly under 21 CFR Part 3 of Subchapter A and Parts 130, 131, 135 through 135g and Parts 141a through 151c of Subchapter C—Drugs were redesignated as Parts 500 through 558 of Subchapter E—Animal Drugs, Feeds, and Related Products.

For the convenience of the user, the following table shows the relationship of the old CFR section numbers under the former Subchapters A and C to the new CFR section numbers in the new Subchapter E, Parts 500 through 558.

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135.22	514.222	135a.18	524.1484g
135.23	514.205	135a.19	524.1580
135.24	514.206	135a.20	524.1883
135.25	514.230	135a.21	524.981e
135.26	514.231	135a.22	524.1044
135.27	514.232	135a.23	524.981d
135.28	514.115	135a.24	524.1862b
135.29	514.120	135a.25	524.1880
135.30	514.121	135a.26	524.2620
135.31	514.15	135a.27	524.1881a
135.32	514.235	135a.28	524.1484a
135.33	514.12	135a.29	555.310c(c)
135.33a	514.11	135a.30	524.1484b
135.34	514.118	135a.31	524.1484d

Old section	New section	Old section	New section
135a.32	524.1484f.	135b.58	522.2662.
135a.33	524.981c.	135b.59	522.204.
135a.34	524.1484c.	135b.60	522.1962.
135a.35	524.402.	135b.61	522.940.
135a.37	524.2640.	135b.62	522.163.
135a.38	548.314b(c).	135b.63	522.1060.
135a.39	524.1484e.	135b.64	522.1680.
135a.40	524.980.	135b.65	522.1662a.
135a.41	524.2140.	135b.66	522.1183.
135a.42	524.1662a.	135b.67	522.1620.
135a.43	524.900.	135b.69	522.883.
135a.44	524.2542.	135b.70	522.723.
135a.45	548.314a(c).	135b.71	522.740.
135a.47	524.541.	135b.72	522.23.
135a.48	524.1881b.	135b.73	522.863.
135a.49	524.660b.	135b.74	522.1404.
135a.50	524.981a.	135b.75	522.2063.
135a.51	524.463.	135b.77	555.210(c).
135a.52	524.981b.	135b.79	522.2404.
135a.56	524.520.	135b.80	522.423.
135a.57	524.1301.	135b.82	522.1731.
135a.58	524.1443.	135b.83	522.54.
135b.2	522.2640.	135b.84	522.1704.
135b.3	522.640.	135b.85	522.1362.
135b.4	522.1940.	135b.86	522.564.
135b.5	522.842.	135b.88	522.281.
135b.6	522.2350.	135b.89	522.1885.
135b.7	522.844.	135b.90	522.1143.
135b.8	522.2340.	135b.91	522.1244.
135b.9	522.2240.	135b.92	522.1880.
135b.10	522.2200.	135b.93	522.1662b.
135b.11	522.1260.	135b.94	522.784.
135b.12	522.2680.	135b.95	522.2582.
135b.13	522.161.	135b.96	540.274c(c).
135b.14	522.961.	135b.97	522.1503.
135b.15	522.2220.	135b.98	540.255a(c).
135b.16	522.1563.	135b.99	522.2444a.
135b.17	522.1380.	135b.100	522.1642.
135b.18	522.1204.	135b.101	522.1820.
135b.19	522.1044.	135b.104	540.207a(c).
135b.21	522.144.	135c.2	546.110c(c) and 546.110d(c).
135b.22	522.62.	135c.3	520.100.
135b.23	522.2120.	135c.4	520.2640.
135b.24	540.280(c)25.	135c.5	520.1660.
135b.25	540.274a(c).	135c.6	520.680.
135b.27	540.265b(c).	135c.7	520.2380a.
135b.28	522.1222.	135c.8	520.2320.
135b.29	522.2480.	135c.9	546.110e(c) and 546.113b(c).
135b.30	522.480.	135c.10	520.2260.
135b.32	522.960.	135c.12	520.2002.
135b.34	522.1020.	135c.13	520.2220a.
135b.35	522.1884.	135c.14	520.2240.
135b.36	522.1462.	135c.15	544.173a(c).
135b.37	522.800.	135c.16	520.2184.
135b.38	522.1182.	135c.17	520.1422.
135b.39	522.2424.	135c.18	520.1242.
135b.40	522.1484.	135c.19	520.2520b.
135b.41	540.207d(c).	135c.20	520.620.
135b.42	522.82.	135c.21	520.1100.
135b.43	540.255c(c).	135c.22	520.1120a.
135b.44	522.1862.	135c.23	520.1840.
135b.45	522.340.	135c.24	520.2122.
135b.46	522.2002.	135c.25	520.2162.
135b.47	522.1720.	135c.26	520.1540.
135b.49	540.274b.	135c.27	520.222.
135b.50	522.1081.	135c.28	520.2200.
135b.51	522.44.	135c.29	520.1962.
135b.52	522.1800.	135c.30	520.62.
135b.53	522.2100.	135c.31	540.129a and 540.129b.
135b.54	522.2444a.	135c.32	520.2123b.
135b.55	522.1920.	135c.33	520.1204.
135b.56	522.2022.		
135b.57	522.380.		

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Old section	New section	Old section	New section
135c.35	548.110(c).	135c.118	540.181b(c).
135c.36	548.114.	135c.119	520.2043.
135c.37	548.112a(c).	135c.120	520.1662.
135c.38	548.110f(c).	135c.121	546.180d(c).
135c.39	520.2520a.	135c.122	546.180c(c).
135c.40	520.2481.	135c.123	546.180a(c).
135c.41	520.2300.	135c.124	546.180b(c).
135c.42	520.2301.	135c.125	546.180e(c).
135c.43	540.174a(c).	135c.127	520.1803.
135c.44	544.170b(c).	135c.128	520.2123a.
135c.45	540.174b(c).	135c.129	520.1120b.
135c.46	520.2220b.	135c.130	540.107a(c).
135c.47	540.107b(c).	135c.131	540.173a(c).
135c.50	520.600.	135c.132	520.2460b.
135c.51	520.139j.	135c.133	540.173b(c).
135c.52	520.622b.	135c.134	520.2160.
135c.53	520.82a.	135c.135	520.1341.
135c.54	520.1801.	135c.136	520.300.
135c.55	520.2460.	135c.137	540.107c(c).
135c.56	520.580.	135d.2	540.829(c).
135c.57	520.1720a.	135d.13	540.874e(c).
135c.58	520.2080.	135d.14	874a(c).
135c.59	520.2045.	135d.15	540.814a(c).
135c.60	520.2380b.	135d.16	540.814(c).
135c.61	520.440.	135d.17	540.874f(c).
135c.62	520.704.	135e.2	558.505.
135c.63	555.110b(c).	135e.5	558.525.
135c.64	520.44.	135e.6	558.55.
135c.65	520.500.	135e.7	558.415.
135c.66	520.1730.	135e.10	558.625.
135c.67	520.182.	135e.18	558.225.
135c.69	520.1802.	135e.26	558.615.
135c.70	520.2022.	135e.31	558.35.
135c.71	520.1920.	135e.34	558.105.
135c.72	540.128c(c).	135e.36	558.630.
135c.73	540.119(c).	135e.39	558.185.
135c.74	520.2280.	135e.43	558.45.
135c.75	520.1720b.	135e.45	558.435.
135c.76	520.1760.	135e.46	558.175.
135c.77	520.260.	135e.49	558.325.
135c.78	520.240.	135e.50	558.355.
135c.79	520.540a.	135e.51	558.195.
135c.81	520.540b.	135e.52	558.25.
135c.82	520.763a.	135e.54	558.205.
135c.83	520.763b.	135e.55	558.575.
135c.84	520.2560.	135e.56	558.305.
135c.85	540.107d(c).	135e.57	558.365.
135c.86	520.622a.	135e.58	558.155.
135c.87	520.82b.	135e.59	558.315.
135c.88	520.2604.	135e.60	558.465.
135c.89	520.863.	135e.61	558.145.
135c.92	520.1900.	135e.63	558.115.
135c.93	520.2362.	135e.64	558.485.
135c.94	520.1263b.	135e.65	558.35.
135c.97	520.23.	135e.66	558.515.
135c.98	520.1284.	135e.67	558.565.
135c.99	555.110c(c).	135e.69	558.635.
135c.100	520.1263a.	135e.1000	558.19.
135c.101	520.1520.	135f.2	529.25.03.
135c.102	555.110a(c).	135f.3	529.1044a.
135c.104	520.1162.	135f.4	529.1044b.
135c.105	520.1320.	135f.5	529.360.
135c.107	520.423.	135g.1	556.1.
135c.108	540.107e(c).	135g.2	556.90.
135c.110	520.1362.	135g.3	556.320.
135c.111	540.105(c).	135g.4	556.70.
135c.112	520.2460a.	135g.5	556.570.
135c.113	520.2582.	135g.6	556.480.
135c.114	520.2100.	135g.7	556.770.
135c.114	544.110(c).	135g.8	556.150.
135c.115	520.784.	135g.9	556.50.
135c.116	520.120.	135g.10	556.300.
135c.117	520.823.	135g.11	556.610.

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Old section	New section	Old section	New section
135g.12	556.510.	141a.27	540.274c(b).
135g.13	556.480.	141a.29	540.274a(b).
135g.14	556.500.	141a.33	540.174a(b).
135g.15	556.740.	141a.35	536.501.
135g.17	556.470.	141a.36	536.502.
135g.18	556.200.	141a.37	536.503.
135g.20	556.280.	141a.38	540.274e(b).
135g.21	556.450.	141a.39	540.250(b).
135g.22	556.260.	141a.42	536.504.
135g.23	556.130.	141a.46	540.274d(b).
135g.24	556.600.	141a.49	536.505.
135g.25	556.430.	141a.54	540.255a(b).
135g.26	556.190.	141a.80	540.274f(b).
135g.27	556.670.	141a.82	540.255c(b).
135g.28	556.540.	141a.83	536.506.
135g.29	556.710.	141a.87	536.507.
135g.30	556.240.	141a.71	540.174b(b).
135g.31	556.140.	141a.74	540.260(b).
135g.32	556.590.	141a.82	540.173a(b).
135g.33	556.60.	141a.86	536.508.
135g.34	556.230.	141a.89	540.380b(b).
135g.35	556.650.	141a.90	540.881(b).
135g.36	556.290.	141a.93	540.874c(b).
135g.37	556.520.	141a.95	536.509.
135g.38	556.250.	141a.97	536.510.
135g.39	556.730.	141a.98	536.511.
135g.40	556.530.	141a.108	540.874b(b).
135g.41	556.380.	141a.109	536.512.
135g.42	556.550.	141b.107	544.373a(b).
135g.43	556.340.	141b.109	544.173a(b).
135g.44	556.210.	141b.111	544.274(b).
135g.45	556.220.	141b.113	544.173b(b).
135g.47	556.120.	141b.115	544.473(b).
135g.48	556.270.	141b.116	544.173e(b).
135g.49	556.370.	141b.117	536.513.
135g.52	556.625.	141b.118	544.211b(b).
135g.53	556.708.	141b.119	536.1708.
135g.54	556.110.	141b.120	544.173d(b).
135g.55	556.660.	141b.122	544.211a(b).
135g.56	556.380.	141b.124	544.170b(b).
135g.57	556.640.	141b.126	544.370b(b).
135g.58	556.700.	141b.128	544.173c(b).
135g.59	556.680.	141b.129	544.373b(b).
135g.60	556.30.	141b.132	544.973b(b).
135g.61	556.410.	141b.134	536.514.
135g.62	556.160.	141b.138	536.515.
135g.63	556.350.	141c.204	546.180a(b).
135g.64	556.780.	141c.205	546.110c(b).
135g.65	556.360.	141c.207	546.110d(b).
135g.67	556.400.	141c.217	546.180e(b).
135g.68	556.420.	141c.219	546.110a(b).
135g.69	556.310.	141c.223	536.516.
135g.70	556.170.	141c.228	546.110b(b).
135g.71	556.20.	141c.237	546.312a(b).
135g.72	556.720.	141c.241	546.110b(b).
135g.73	556.690.	141c.256	546.110g(b).
135g.75	556.180.	141c.264	539.210d.
135g.76	556.490.	141c.265	546.113a(b).
135g.77	556.630.	141c.267	539.210b.
135g.79	556.440.	141c.268	536.517.
135g.80	556.300.	141d.303	555.310c(b).
135g.81	556.100.	141e.403	548.212(b).
135g.82	556.560.	141e.416	539.310b.
135g.83	556.40.	141e.417	548.112d(b).
135g.84	556.380.	141e.422	548.310b.
135g.85	556.580.	141e.423	548.112a(b).
135g.89	556.750.	141e.425	548.110(b).
141a.8	540.380a(b).	141e.426	548.112b(b).
141a.9	540.173b(b).	141e.427	548.113(b).
141a.19	540.281b(b).	141e.428	548.112c(b).
141a.21	540.180a(b).	141e.429	536.518.
141a.22	536.500.	141e.431	548.111(b).
141a.23	540.281a(b).	144.11	510.505.

Redesignation Table No. 1

Old section	New section	Old section	New section
44.25	510.510.	148b.123	544.173c(a).
44.26	510.515.	148b.124	544.373b(a).
46.2	514.50.	148b.127	544.973b(a).
46.3	514.51.	148c.204	546.180a(a).
46.4	514.150.	148c.205	546.110c(a).
46.5	510.350.	148c.206	546.312b(a).
46.6	514.155.	148c.207	546.110d(a).
46.8	514.60.	148c.208	546.481(a).
46.9	514.160.	148c.212	546.713(a).
46.13	514.55.	148c.217	546.180e(a).
46.15	514.210.	148c.219	546.110a(a).
46.16	514.11.	148c.222	546.180f(a).
46a.24	540.280(a).	148c.228	546.110f(a).
46a.26	540.380a(a).	148c.237	546.312a(a).
46a.27	540.173b(a).	148c.241	546.110b(a).
46a.28	540.181a.	148c.244	546.381a(a).
46a.34	540.153(a).	148c.246	546.381b(a).
46a.39	540.174c(a).	148c.256	546.110g(a).
46a.41	540.281a(a).	148c.254	539.210b.
46a.43	540.253.	148c.265	546.113a(a).
46a.45	540.274c(a).	148c.267	539.210a.
46a.47	540.274a(a).	148d.303	555.310c(a).
46a.49	540.163(a).	148d.304	555.310a.
46a.51	540.174a(a).	148d.308	555.310b. and 555.410.
46a.53	540.180a(a).	148e.401	539.310c.
46a.57	540.274e(a).	148e.402	548.313b.
46a.58	540.250(a).	148e.403	548.212(a).
46a.61	539.73.	148e.408	548.310a(a).
46a.62	540.874c(a).	148e.416	539.310a(a).
46a.65	540.265a.	148e.417	548.112d(a).
46a.66	540.265b(a).	148e.423	548.112a(a).
46a.67	540.274d(a).	148e.425	548.110(a).
46a.68	540.155(a).	148e.426	548.112b(a).
46a.75	540.261.	148e.427	548.113(a).
46a.77	540.255a(a).	148e.428	548.112c(a).
46a.80	540.259.	148e.430	548.313a.
46a.84	540.274f(a).	148e.431	548.111(a).
46a.86	540.255c(a).	148.2	510.45.
46a.88	540.180b.	148.3	510.55.
46a.93	540.174b(a).	148.5	510.106.
46a.95	540.160(a).	149a.14	540.119.
46a.96	540.260(a).	149b.17	540.107b.
46a.98	540.166(a).	149b.19	540.207.
46a.100	540.255b.	149b.21	540.107d.
46a.104	540.173a(a).	149b.23	540.107e.
46a.111	540.380b(a).	149b.24	540.105.
46a.112	540.881(a).	149b.26	540.107a.
46a.126	540.874b(a).	149b.27	540.207a.
46a.129	540.874f.	149b.28	540.107c.
46b.101	539.170c.	149c.6	540.129b.
46b.102	544.373a(a).	149c.7	540.129a.
46b.104	544.173a(a).	149c.8	540.129c.
46b.105	544.370a.	149c.10	540.829.
46b.106	544.274(a).	149j.1	540.114a.
46b.107	544.170a.	149j.2	540.114.
46b.108	544.173b(a).	149j.11	540.814a.
46b.110	544.473(a).	149j.12	540.814.
46b.111	544.173e(a).	151c.12	555.110b.
46b.113	544.211b(a).	151c.14	555.310g.
46b.114	539.170a.	151c.16	555.310e.
46b.115	544.173d(a).	151c.18	555.310d.
46b.117	544.211a(a).	151c.19	555.210.
46b.119	544.170b(a).	151c.20	555.110c.
46b.121	544.370b(a).	151c.21	555.110a.

Redesignation Table No. 2

At 40 FR 14156, March 28, 1975, as amended at 40 FR 26027, June 20, 1975, a document was published which transferred and reorganized regulations on tolerances for pesticides in animal feeds administered by the Environmental Protection Agency. The regulations formerly codified in 21 CFR Part 121 were transferred to Part 561.

The following table shows the relationship of former CFR section numbers and the new section numbers assigned to them.

Old section	New section	Old section	New section
121.204.....	561.210	121.330.....	561.30
121.211.....	561.230	121.331.....	561.240
121.215.....	561.160	121.332.....	561.280
121.216.....	561.110	121.334.....	561.280
121.218.....	561.220	121.335.....	561.280
121.221.....	561.130	121.336.....	561.150
121.226.....	561.120	121.337.....	561.250
121.227.....	561.370	121.338.....	561.80
121.228.....	561.270	121.339.....	561.60
121.240.....	561.180	121.340.....	561.350
121.260.....	561.380	121.341.....	561.400
121.270.....	561.260	121.342.....	561.140
121.274.....	561.70	121.343.....	561.50
121.281.....	561.40	121.344.....	561.190
121.287.....	561.365	121.345.....	561.330
121.289.....	561.310	121.346.....	561.300
121.290.....	561.340	121.347.....	561.290
121.296.....	561.290	121.348.....	561.80
121.300.....	561.100	121.349.....	561.20
121.303.....	561.410	121.350.....	561.320
121.326.....	561.170	121.351.....	561.235

Redesignation Table No. 3

At 41 FR 10984, March 15, 1976, regulations formerly under Part 121 of Subchapter B—Food and Food Products, were redesignated and transferred into Parts 526, 529, 540, and 558 of Subchapter E—Animal Drugs, Feeds, and Related Products.

For the convenience of the user, the following table shows the relationship of the old CFR section numbers under Part 121 to the new CFR section numbers reflected in Parts 526, 529, 540, and 558.

Old section	New section	Old section	New section
121.206	558.3	121.253	558.62
121.207	558.680	121.254	558.60
121.208	558.128	121.255	558.262
121.210 and 558.55	558.55, and 558.58	121.265	558.480
121.213	558.274	121.258	558.240
121.220	558.430	121.262 and 558.530	558.530
121.233	558.78	121.263 and 121.264	558.376
121.237	558.368	121.267	558.266
121.298	558.126	121.280	558.579
121.241 and 558.225	558.225	121.292 and 558.248	558.248
121.248	558.370	121.297	558.258
121.249	526.820, 526.1014, 529.2080, 540.874d(c), and 540.874g	121.305	558.582
121.251	558.450	121.308	558.342
121.252	558.76	121.310	558.120
		121.323	558.254

Redesignation Table No. 4

At 41 FR 38618, September 10, 1976, provisions under Parts 1 and 3 of Subchapter A and Parts 10, 90, 102, 121, 122, and 128b of Subchapter B were redesignated as Parts 501, 503, 507, 508, 509, 564, 570, 571, 573, and 582 of Subchapter E—Animal Drugs, Feeds, and Related Products.

For the convenience of the user, the following table shows the relationship of the CFR section numbers under Subchapters A and B to the redesignation reflected in Parts 501, 503, 507, 508, 509, 564, 570, 571, 573, and 582.

Old section		New section	
1.7	501.1	121.3	570.30
1.8	501.3	121.4	570.18
1.8a	501.5	121.5	570.22
1.8b	501.105	121.6	570.20
1.8c	501.15	121.11	570.6
1.8d	501.8	121.40	570.35
1.9	501.2	121.41	570.38
1.10	501.4	121.51 except pars. (k) and (l)	571.1
1.10a	501.100	121.51 pars. (k) and (l)	571.100
1.10b	501.103	121.52	571.7
1.12	501.17	121.53	571.6
1.13	501.22	121.54	571.102
1.15	501.18	121.55	571.110
1.16	564.8	121.56	571.200
3.93	564.20	121.57	571.203
10.1	509.15	121.58	571.202
10.2	564.3	121.59	571.120
10.3	564.5	121.60	571.204
10.4	501.110	121.61	571.220
10.5	564.17	121.62	571.221
10.6	564.12	121.63	571.222
10.7	564.14	121.64	571.205
10.8	564.6	121.65	571.206
90.1	508.3	121.66	571.208
90.2	508.19	121.67	571.210
90.3	508.5	121.68	571.212
90.4	508.7	121.69	571.214
90.5	508.10	121.70	571.230
90.6	508.6	121.71	571.232
90.7	508.12	121.72	570.15
90.20	508.35	121.73	571.235
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121.101(e)(4).....	582.40
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121.101(g).....	582.80
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121.209.....	573.180
121.210.....	573.480
121.222.....	573.1000
121.223.....	573.700
121.224.....	573.640
121.229.....	573.940
121.230.....	573.420
121.231.....	573.300
121.234.....	573.600
121.235.....	573.860
121.236.....	573.840
121.239.....	573.780
121.242.....	573.660
121.246.....	573.660
121.247.....	573.580
121.250.....	573.260
121.261.....	573.720
121.265.....	573.320
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121.273.....	573.900

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121.283.....	573.980
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121.285.....	573.180
121.286.....	573.620
121.288.....	573.120
121.295.....	573.780
121.298.....	573.440
121.301.....	573.540
121.302.....	573.200
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121.307.....	573.880
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128b.8.....	507.110
128b.9.....	507.89
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Redesignation Table No. 5

At 53 FR 24666, June 29, 1988, 21 CFR Part 561 was redesignated as 40 CFR Part 186. The following redesignation table shows the relationship of the CFR section numbers formerly in 21 CFR Part 561 and those sections being redesignated as 40 CFR Part 186.

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561.20	186.100	561.260	186.3700
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561.40	186.200	561.268	186.3800
561.41	186.250	561.270	186.3850
561.50	186.350	561.273	186.4000
561.51	186.375	561.280	186.4050
561.53	186.4975	561.282	186.4150
561.60	186.450	561.283	186.4450
561.65	186.500	561.285	186.4575
561.66	186.550	561.289	186.4700
561.67	186.600	561.290	186.4750
561.70	186.700	561.300	186.4800
561.80	186.750	561.305	186.4850
561.91	186.950	561.310	186.4900
561.92	186.400	561.330	186.5000
561.93	186.800	561.340	186.5200
561.95	186.850	561.350	186.5350
561.96	186.1250	561.360	186.1550
561.97	186.1300	561.365	186.5400
561.98	186.1000	561.367	186.5550
561.99	186.1400	561.385	186.5600
561.100	186.1450	561.386	186.5650
561.110	186.1500	561.387	186.5700
561.130	186.1600	561.390	186.5800
561.140	186.1650	561.400	186.1350
561.145	186.1700	561.410	186.6300
561.150	186.1675	561.415	186.1750
561.160	186.1950	561.420	186.2000
561.170	186.2100	561.425	186.2050
561.180	186.2225	561.427	186.1800
561.190	186.2325	561.428	186.3250
561.191	186.2150	561.429	186.3650
561.197	186.2275	561.430	186.2800
561.200	186.2400	561.432	186.4950
561.210	186.2450	561.434	186.5100
561.215	186.2500	561.435	186.3300
561.220	186.2550	561.436	186.3400
561.225	186.2700	561.437	186.1050
561.230	186.2750	561.438	186.3200
561.232	186.2950	561.439	186.1100
561.233	186.3000	561.440	186.1850
561.234	186.3050	561.441	186.300
561.235	186.2775	561.442	186.5950
561.240	186.3350	561.443	186.4350
561.250	186.3450	561.444	186.5850
561.253	186.3500	561.445	186.5250
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All changes in this volume of the Code of Federal Regulations which are made by documents published in the FEDERAL REGISTER since March 27, 1975, are enumerated in the following list. Entries indicate the nature of the changes effected. Page numbers refer to FEDERAL REGISTER pages. The user should consult the entries for chapters and parts as well as sections for revisions.

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561.283 Added.....	14897
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